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SOME OBSERVATIONS ON THE FIFTH AND SEVENTH CRANIAL NERVES.

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THE present inquiry was begun because Dr. Hinds Howell placed at our disposal a number of cases of trigeminal neuralgia which he had treated by alcoholic injection of the Gasserian ganglion. A study of such cases, it was thought, would enable us to compare the anatomical and physiological results of this form of treatment with that of surgical removal of the Gasserian ganglion.

It is unnecessary to re-state the clinical position in regard to the injection or the surgical methods of treatment, but we wish to present evidence in what follows for asserting that the whole Gasserian ganglion can be permanently destroyed by an injection of alcohol. Further, it was hoped that in the course of such a study we might investigate once more the many problems appertaining to the cranial nerves still left unsolved, despite the many excellent and thorough investigations already published. Some of the problems that interested us were the anatomy of the taste nerves, the anatomy and physiology of deep pressure pain, the course and distribution of the proprioceptive fibres in the ocular and facial muscles and with this, the problem as to whether such fibres can give rise to the sensation of pain, and the existence of accessory pathways for pain.

[1] This article formed the basis of one of the Oliver-Sharpey Lectures at the Royal College of Physicians, London, 1933.

General Remarks on the Fifth Nerve.

At the outset we offer a few observations on the general biological position of the fifth nerve in order to obtain some perspective of the nature and quality of the cranial nerves.

In a relative sense the anatomy and physiology of the fifth nerve are well known. The gradual evolution of the nerve through the representatives of all the main classes of vertebrates has been traced. Such studies have made it clear that the nerve is of a two-fold nature, the ophthalmicus being one part and the maxillo-mandibularis the other. Kappers [22] has identified these two nerves in amphioxus where they are quite separate. In the cyclostomes (Johnston [20]), the next lowest vertebrates after amphioxus, the two nerves have fused and a descending intra-medullary tract belonging to the ophthalmicus is present in the brain-stem. It is doubtful, however, if an ascending mesencephalic root exists. In all higher forms the ascending mesencephalic root and the descending root are present and, when we reach the reptiles, the nerve is morphologically complete. The mesencephalic root in these extends cranially into the tectum, and a principal nucleus is present which gives crossed fibres to the mesial fillet as well as a descending root contributing crossed fibres to the spinothalamic tract. In all classes of vertebrates the ophthalmicus is the main constituent of the descending root; it runs ventral to the maxillo-mandibularis portion of the root and reaches further caudally than these. This descending root of the ophthalmicus comes into association with motor centres of the spinal cord, as those for the pectoral fins in fishes, those for the fore-limbs in the amphibia, in the frog it even reaches the lumbar enlargement, and those for the cervical muscles in man. The maxillo-mandibularis portion is connected more closely to the branchial system of nerves and the connections of its descending roots are intimate with the seventh, ninth and tenth cranial nerves.

Comparative anatomy indicates that the functions of crude sensation of the nerve precede those of a discriminating quality, the latter not appearing until the reptiles are reached (Brouwer [5], Johnston [19], Herrick [18], Woollard [32] *et alia*). When the nerve can first be identified it is the great somatic sensory nerve of the head region. The ophthalmicus innervates the post-axial region of the head, i.e., the dorsum, starting from the tip of the nose, which is the true front end of the body, while the maxillo-mandibularis functions as the somatic sensory component for all the remaining cranial nerves which contain no such fibres except the vestiges of those formerly innervating the

lateral line system. This lateral line system, which subserves a variety of tactile sense by means of which the swimming animal became aware of the swish of the water along its body, disappeared when vertebrates became terrestrial and the remains of the nerves belonging to it became clustered around the external auditory meatus as the auricular nerve of Arnold, this being made up of small fasciculi from the seventh, ninth and tenth cranial nerves.

The fact that the fifth contributes to the innervation of the mouth might suggest that its range is not confined to cutaneous areas. The vertebrate mouth is, however, a new formation and the fifth becomes involved in it secondarily while still keeping its cutaneous quality. On phylogenetic grounds it is improbable that the fifth should carry impulses subserving taste.

The opthalmicus is then a purely cutaneous nerve with its own history and running its own course in the development of each vertebrate. In human development it runs in the mesenchyme that invests the head, viz., the paraxial mesoderm, and centrally it gives off the long descending tract ultimately connected with the spinal motor centres. It is thus the basis of protective reflexes, made more important by the fact that it is the front nerve of the body. The maxillo-mandibularis is related to the first branchial arch and the nerve is embedded in the mesenchyme of the arch, thus differing from the ophthalmicus. Its descending root is, as is to be expected, more intimately related to the other branchial nerves, and it is with the seventh, ninth and tenth that it establishes its medullary connections.

It is to be remembered that the cranial nerves are not modified spinal nerves, but a system which is much older and simpler than these. It is now agreed that the fundamental divisions of the body determined on comparative embryological grounds by Brachet [4] are well founded. The first and oldest portion of the body is the region of the fore-brain vesicle with the olfactory and optic systems and the front end of the pharynx with adjacent structures. It is for this region that the opthalmicus becomes the somatic sensory receptor beginning, and indeed continuing, for the most part to act as the nerve for sensations of a crude quality. The second oldest part of the body is the region corresponding to the brain-stem between the fifth and tenth nerves, and including the branchial apparatus. Here the cranial nerves proper are situated. It is a region where segmentation is transient, doubtful and obscure. The remaining portion of the body, the trunk and the tail with the organs of locomotion and the genito-urinary structures, appears

last; it is characterized by a high degree of segmentation, no special sense organs are developed in it and the spinal nerves become aggregated into bundles containing all the afferent and efferent fibres of each segment. The cranial nerves, on the contrary, are more primitive and do not show this combination of all the components, for the ventral and dorsal roots remain separate. The dorsal roots are for the most part mixed nerves but, nevertheless, the older cranial nerves tend to confine each function to different nerves. They must be studied as a special class by themselves, and for the reasons just given they might be expected to offer greater opportunity for unravelling the functions of the peripheral nervous system. The tendency for the cranial nerves, as the fifth, to form descending roots, also distinguishes them. It is in strong contrast with the spinal nerves, and even if neurobiotaxis be the explanation it can still be emphasized as a special character of nerves in the region of the brain-stem.

The mesencephalic root of the fifth is another case of functional segregation in the cranial nerve region (Johnston [21]). Every muscle has its sensory innervation, and it seems definite from experimental investigation (Allen [1]) that the mesencephalic root contains cells the axones of which pass out in the sensory root of the fifth and then traversing the ganglion, but not using its cells, enter the mandibular branch to reach the muscles of mastication. Evidence has been brought forward that this mesencephalic root may be the source of proprioceptive fibres for the masticatory muscles, and perhaps for the ocular muscles (Woollard [31]). The cranial extension of this nucleus, its advance in the mid-brain even to the level of the posterior commissure in man and its proximity to the ocular nuclei, are in accord with such probabilities.

The inclusion of the mesencephalic root in the brain-stem is unexpected, for cells elsewhere performing a similar function are lodged in the dorsal root ganglia. The neural crest from which the Gasserian ganglion is derived is formed at the level of the mid-brain and from the most anterior of the neuromeres of the hind-brain (Van Wijhe [29], Bartlemez and Evans [2]). It may be supposed that the more anterior part of the neural crest, instead of advancing laterally, becomes incorporated in the brain-stem. This incorporation may be in some way concerned with the fact that the mesencephalon is at the junction of anterior and middle constituents of the body as described previously. It has also been suggested that the mesencephalic nucleus is homologous with the large sensory cells which in lower vertebrates lie within the central nervous system and send axones to the muscles and skin. For neither of these hypotheses is there any adequate proof at the moment.

Material.—We had twenty cases of trigeminal neuralgia at our disposal; in all but two, who had the ganglion removed by open dissection ten or more years previously, an alcoholic injection of the Gasserian ganglion had been performed by Dr. Hinds Howell. In several instances we had the opportunity of examining the patients both before and after the injection. Twelve cases of facial palsy, due to lesions at various levels of the nerve, and five cases in which the cervical sympathetic had been removed or injured on one or both sides were included in the investigation.

The Extent of the anæsthesia.—There is no need to dwell at length on the area from which sensation disappears after destruction of the Gasserian ganglion. Such studies have been published many times and the results of various methods compared—Bolk [3] by the method of dissection, Davies [8] and Cushing [7] after removal of the ganglion, Harris [17] after alcoholic injection. The results obtained by these various methods agree closely. We have found that in the complete cases, ten of the eighteen, investigated by us after alcohol injection the area of anæsthesia resembled in every detail that which follows surgical removal (figs. 1, 2 and 3). The backward prolongation to the ear with the inclusion of the anterior and superior walls of the external auditory meatus and the tympanic membrane may be noted. The area in front of the angle of the jaw is excluded and the line of the anæsthesia drops near the angle of the mouth to the lower border of the ramus of the jaw. In the mouth all the hard and soft palate and the upper half of the anterior pillar of the fauces are included. On the tongue the anæsthesia ceases in front of the vallate papillæ, these falling within the area of the glosso-pharyngeal nerve.

Like Davies and Cushing we have found that the anæsthesia is often coincident for all forms of sensation, but when such is not the case the tactile loss has usually been the most extensive. We have had little opportunity of studying the recession of the anæsthesia that Davies commented on. In those of our series in whom the ganglia had been destroyed for the longest periods the area of anæsthesia was in no way less than those in whom the ganglion had but recently been injected. In ten of the eighteen cases injected with alcohol there was a complete loss of all forms of cutaneous sensation over the distribution of the fifth nerve. The longest period since the injection was ten years, the shortest a few weeks, and in all the relief from pain was complete. We feel that the examination of these cases favours the view that by means of alcoholic injection the relief from pain is equal to, and the area of anæsthesia is as complete, as that following surgical treatment.

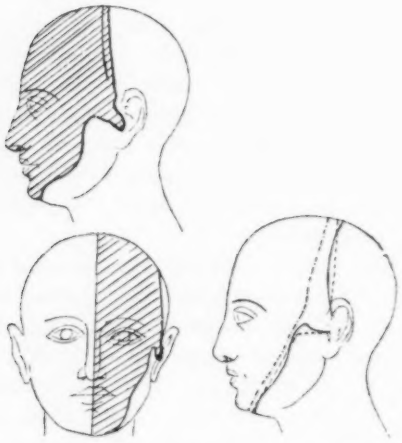

FIG. 1.—Area of anæsthesia after surgical removal of Gasserian ganglion. (Cushing.)

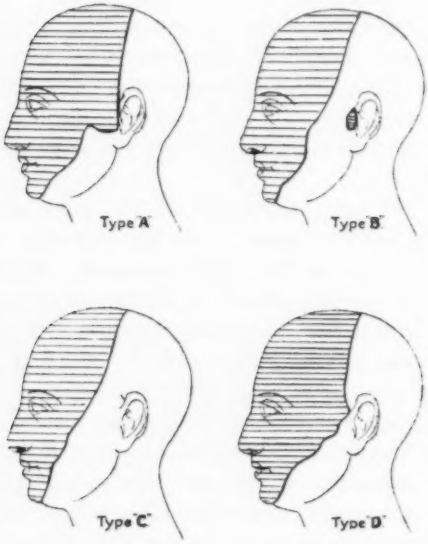

FIG. 2.—Area of anæsthesia after surgical removal of Gasserian ganglion. (Davies.)

Referred pain.—There is evidence that headaches may arise through stimulation of the nerve endings in the dura mater; the precise nature of the stimulus is uncertain (Pickering and Hess [25]). The dura of the anterior and middle cranial fossæ, together with the tentorium cerebelli, receive their innervation from the fifth nerve and particularly from the ophthalmic branch. We asked particularly many patients about the occurrence of headache and from some we got the emphatic assertion that they did suffer from headaches on the anæsthetic side. Records as to headache were made in 12 cases: 7 never had any headache, 1 case suffered with headache only on the non-anæsthetic side, while 4 patients

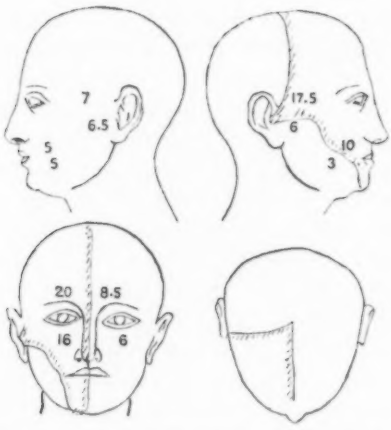

FIG. 3.—Area of anæsthesia after alcoholic injection of the ganglion by Hinds Howell. Algometric readings are indicated.

were definite that their headaches were felt on both sides of the head. In 2 of these 4 cases the cutaneous area of anæsthesia was complete, but incomplete in the other 2. This suggests that all headaches may not arise through the dural nerves and that headache may arise centrally and be referred to the peripheral distribution of the fifth.

Pain reflexes.—The conjunctival reflex is, of course, abolished and the oculo-cardiac reflex, we believe, is absent too. In testing this reflex upon ourselves we found that it was elicited by a degree of pressure on the globe of the eye which was painful, and not until pain was experienced were we able to detect in polygraph tracings any slowing of the heart. We were reluctant to exert this amount of pressure upon the patients investigated, but we came to the conclusion that ocular pressure pain

was absent in those who had been deprived of the Gasserian ganglion, In the five cases examined we were unable to obtain the oculo-cardiac reflex from the anæsthetic side; in two of these cases the anæsthesia was on the left side, in the remainder on the right. All the evidence indicates that pain is the only common sensation in the eye-ball. The optic nerve subserves its special function only, the ophthalmic is the afferent limb of protective reflex arcs aroused solely by pain, while the autonomic nerves regulate the amount of light entering the eye by alterations of the size of the pupil.

Taste.—We have taken the occasion to observe the effect of these injections on taste and have met with the same discrepancies which have vexed all other observers. The published investigations show that in about half the cases the taste is unimpaired and in about half it is lost. The reasons put forward to explain the loss of taste have been for the most part anatomical. Thus it has been suggested that the ninth nerve was the sole nerve of taste; that taste first travelled peripherally in the chorda tympani and from there was transmitted through the small superficial petrosal nerve and otic ganglion to the mandibular nerve; that taste impulses were transmitted from the chorda tympani through the great superficial petrosal and spheno-palatine ganglion to the maxillary division of the fifth; that taste travelled back through the chorda tympani and small superficial petrosal and thence to Jacobsen's nerve and the glossopharyngeal and so centrally. These anatomical explanations have always seemed improbable: the chorda tympani and pars intermedia is the most obvious route, though this route does not account for the large number of cases in which taste appeared to be impaired following destruction of the Gasserian ganglion. To account for these Dixon [11] brought forward evidence that the extirpation of the ganglion might readily be accompanied by injury to the seventh nerve, by way of the hiatus Fallopii. We repeated the experiment of injecting the ganglion in the cadaver by means of coloured gelatine solutions in order to find where such injections would most readily spread (fig. 4). This showed that injected material spread along the central root of the fifth into the posterior fossa, over the cerebellar hemisphere and through the hiatus Fallopii to the position of the geniculate ganglion. Dixon's suggestion is therefore not improbable, but in all our cases careful note was made of the condition of the seventh nerve and no impairment of its function was ever discovered in those where taste was absent. It may be that the cells of the geniculate ganglion are more readily affected by the alcohol than the motor fibres of the seventh, though we know of no evidence that this is so.

In our series of seventeen cases in which it was possible to test taste satisfactorily by applying test substances to the protruded tongue, ten had a complete loss on the anæsthetic side, taste being preserved on the normal side. Evidence of loss was accepted only when the substance had been applied for not less than thirty seconds and then did not produce a sensation. In several of these ten cases the injection had been performed over a year previous to the time of testing. Seven cases retained the sensation of taste. We can offer no satisfactory explanation as to why taste should sometimes persist and sometimes be lost after

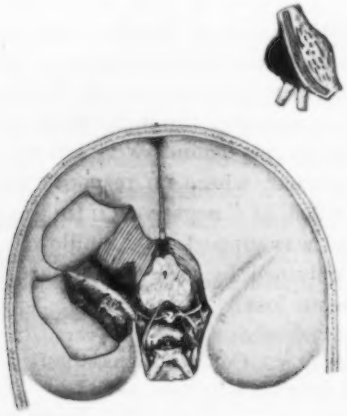

FIG. 4.—Dissection showing the spread of coloured gelatine injected into the Gasserian ganglion post mortem. The spread over the cerebellum and to geniculate ganglion is shown, together with the mass in the Gasserian ganglion.

destruction of the Gasserian ganglion. It cannot be explained by the well-known variability of gustatory acuity of the anterior two-thirds of the tongue, since in our cases in which taste was lost on the one side, it was present on the opposite side. Leakage of the injected solution towards the geniculate ganglion undoubtedly does occur; and this explanation of the loss of taste would be satisfactory if one could have detected other evidence indicating impairment of the seventh nerve. In the cases of facial palsy we examined, taste was lost in some and present in others, but most of the cases had peripheral lesions and therefore involvement or escape of the chorda tympani would explain this variation. In three

cases of intracranial lesions of the seventh nerve, as by acoustic nerve tumours, taste was absent. Though the evidence in favour of the seventh nerve carrying taste fibres, evidence which is derived from comparative anatomy, experimental inquiry and clinical observation, seems decisive enough, the loss of taste in so many of these fifth nerve cases is very puzzling, and we feel that no satisfactory explanation has yet been obtained

Deep pressure pain.—Deep pressure pain was investigated by means of an algometer. This instrument consists of a rod balanced against a spring graduated to read in pounds; the blunt extremity of the applicator is three-eighths of an inch in diameter (9 5 mm.). In applying this instrument a gradually increasing pressure was exerted at right angles to the area being tested, the patient keeping his eyes closed. The patient was instructed to respond by raising his hand as soon as he felt the pressure becoming painful; the instrument was then removed and read. Pressures over twenty pounds were not attempted owing to the danger of injuring tissues; where no response was made with such a pressure it was recorded as "negative." In the early stages of this investigation the head was supported by a pillow.

Typical readings obtained by this method are illustrated in a case with complete cutaneous loss:

Mrs. C.—Trigeminal neuralgia for several years. Injection of alcohol 1930. Examination two years later. Cutaneous anæsthesia complete. Symmetrical points were tested and gave the following results:—

	Normal side	Anæsthetic side
Temporal fossa	4 lb.	5 lb.
Supra-orbital region	4 lb.	10 lb.
Above zygoma	6 lb.	6 lb.
Masseter (non-anæsthetic on both sides)	5 lb.	4 lb.

Many readings similar to this case were obtained, and at first we were inclined to assume that deep pressure pain could still be elicited over the anæsthetic area, and it was natural to infer that the seventh nerve would afford the most likely anatomical pathway for such sensation. Similar investigations and conclusions have been published by others, e.g., Frazier [14], Davis [10], Gerard [16], Maloney and Kennedy [24] *et alia*, and the figures they give are of a similar order to those presented by us.

Our confidence in this interpretation was disturbed when we encountered cases in which the readings were of such an order as to suggest that deep pain was absent when the fifth nerve only was destroyed, and seventh nerve intact, as in the following case :—

Mr. F.—Alcohol injection for trigeminal neuralgia in 1923, and complete anæsthesia of the trigeminal area when investigated in 1932, that is nine years later. An investigation of deep pressure pain with the algometer gave the following readings:—

	Normal side	Anæsthetic side
Supra-orbital region	7 lb.	Negative
Infra-orbital region	8 lb.	18 lb.
Temporal fossa	9 lb.	6 lb.
Masseter (non-anæsthetic on both sides)	9·5 lb.	9·5 lb.

The discrepancy in the readings from the temporal region led us to reconsider our technique. On re-testing the temporal region with the head firmly supported the readings obtained were:—

	Normal side	Anæsthetic side
Temporal fossa	8 lb.	11·5 lb.

This indicated the importance of eliminating the action of the cervical muscles, and thereafter deep pressure was reinvestigated in several of the earlier cases and in all others while the head was voluntarily pushed hard against a rigid resistance. When this was done we found that deep pressure pain could not be elicited over the anæsthetic area. The following cases illustrate this:—

J. R.—Injected with alcohol in September, 1931. Investigated January, 1932. Anæsthesia complete. The following readings were obtained, the head not being held properly rigid:—

	Normal side	Anæsthetic side
Temporal fossa	5 lb.	8 lb.
Supra-orbital region	4 lb.	17 lb.

When the activity of the cervical muscles was excluded by the head being pressed hard against a rigid resistance, the following readings were obtained:—

	Normal side	Anæsthetic side
Temporal fossa	5 lb.	Negative
Supra-orbital region	6 lb.	Negative
Infra-orbital region	7·5 lb.	Negative

Mrs. C.—Injected March, 1932. Examined one year later. The anæsthesia was complete.

The first set of readings obtained with head improperly supported were:—

	Normal side	Anæsthetic side
Temporal fossa	4 lb.	5 lb.
Supra-orbital region	4·5 lb.	10 lb.

When re-tested with careful control of the cervical muscles the result was:—

Temporal fossa	7 lb.	17·5 lb.
Supra-orbital region	4 lb.	Negative

In eight cases results similar to these experiences were obtained and we began to favour the conclusion that the fifth nerve contained the

fibres of deep pressure pain the appreciation of which was lost when the ganglion was destroyed. This impression was confirmed by our observations on deep pressure pain over the buccinator. The method adopted was to press the algometer against the outside of the cheek which was supported on the inside by the observer's fingers. By this means we felt justified in believing that the patient could obtain no impression of the amount of pressure exerted through the instrument except from the region to which the instrument was applied. The line of cutaneous anæsthesia crosses the buccinator, and unless care is taken to ascertain that the applicator is in contact with anæsthetic skin the readings may be low, and in crossing the line between the non-anæsthetic and anæsthetic areas over the buccinator there is the greatest difference in the readings. For example, in one case the anæsthetic area over the buccinator gave a reading of over 11 lb., while close by where the skin was non-anæsthetic (falling outside the trigeminal area) the reading was 6 lb.; in another case the same procedure gave 11 lb. over the anæsthetic part and 2 lb. over the adjacent normal area. Thus confirmation was obtained that the fifth nerve subserves the function of deep pain from the face area.

To test this conclusion further the seventh nerve was blocked by injection in five cases. The needle was inserted just in front of the tip of the mastoid process to a depth of about 1·5 cm., and 3 c.c. of 4 per cent. novocain and 1 in 60,000 adrenalin were injected. Complete facial palsy was regarded as adequate evidence of total blocking of the seventh nerve for, as is well known, sensation disappears before the motor loss is observed in such injections. The algometric readings in such cases were in no way altered from readings obtained before the injection of the seventh nerve. An illustrative case is that of E.B.:—

Injected 1932. Complete loss over the maxillary and mandibular areas, partial in the region of the ophthalmic branch. In the anæsthetic region, the algometer readings were:—

	Normal	Anæsthetic
Infra-orbital region	6·5 lb.	Negative
Temporal fossa	4·5 lb.	Negative
Supra-orbital region (partial anæsthesia)	3·5 lb.	5·5 lb.

The facial nerve was then injected with 4 per cent. novocaine and 1 in 60,000 adrenalin, with a resulting complete facial palsy, and the following readings were obtained:—

	Normal	Anæsthetic
Infra-orbital region	4·5 lb.	Negative
Temporal fossa	4·5 lb.	Negative
Supra-orbital region	3·5 lb.	7 lb.

The addition of a facial block in no way affected the readings over the maxillary and mandibular distributions, and it is interesting to observe that in the distribution of the ophthalmic, where the anæsthesia was only partial, the injection of the seventh nerve gave no significant alteration in the reading for deep pressure pain.

Another series of observations support the suggestion that the fifth nerve carries the impulses recognized as deep pressure pain. In twelve cases of facial palsy due to lesions varying in situation from the stylo-mastoid foramen to the internal ear, algometric readings on the side of the facial paralysis in no way differed from those obtained on the healthy opposite side.

TABLE OF ALGOMETRIC READINGS IN FACIAL PALSY OF EIGHT YEARS DURATION (FIFTH INTACT).

	Normal	Palsied side
Supra-orbital region	8 lb.	8·5 lb.
Infra-orbital region	9 lb.	8 lb.
Buccinator	9·5 lb.	10 lb.
Temporal fossa	8·5 lb.	7·5 lb.

From these several observations we conclude that the fifth nerve is the pathway for deep pressure pain from the face area, thus confirming an opinion expressed earlier by Wilfred Harris [17].

Afferent fibres in the seventh nerve.—The investigations recounted in the previous section brought us to the conclusion that the impulses of deep pressure pain run in the fifth nerve; this raised accordingly the problem as to the existence of afferent fibres in the seventh nerve, other than those for taste and, if present, what functions they subserved.

The presence of afferent fibres in the seventh nerve has been demonstrated by chromatolytic methods and degeneration experiments (v. Gehuchten [28], Edgeworth [12], Edgeworth and Wakeley [30]). When the fifth is destroyed no ataxia of the ocular muscles has ever been recorded; it can also be shown that no ataxia of facial muscles can be detected. The absence of ataxia of the facial muscles is demonstrable by the fact that our cases with complete destruction of the motor and sensory portions of the fifth nerve were able to carry out alternating movements of the two sides of the face with precision, and could repeat on the anæsthetic side any movement which they had been instructed to carry out on the normal side. Though such patients were unaware of the accumulation of food against the anæsthetic cheek, yet they recognized the displacement if this was brought about quickly by pushing against its inner and anæsthetic surface with a blunt instrument. We were able to demonstrate this satisfactorily in twelve cases; and in four

cases the pinching up and stretching rapidly of the anæsthetic skin over the face was immediately appreciated. When the seventh nerve was blocked and a facial palsy induced, these patients were unable to apprehend the distension of the cheek. For these reasons we believe that the afferents in the facial, other than those of the chorda tympani, subserve proprioceptive sensibility, and from our previous observations we further conclude that these fibres do not carry impulses of deep pressure pain.

Paræsthesia.—Three cases who had a complete loss of function of the fifth nerve suffered from paræsthesia of a burning and distressing character. In two of these cases the ganglion had been removed at operation eleven and twelve years previously with a resulting complete anæsthesia to all recognized tests over the face, nose and mouth. These two cases do not lend support to the suggestion that the paræsthesiæ only occur in cases with incomplete destruction of the ganglia. Attempts were made to relieve the distressing subjective sensations by blocking the seventh nerve at the stylo-mastoid foramen with novocain, but no alteration in their character or intensity resulted therefrom.

Blushing.—It was found that blushing produced by means of suitable stimuli was symmetrical and equal on the two sides of the face in cases with the Gasserian ganglion previously destroyed. The ability to blush equally on both sides of the face was observed in three cases with unilateral cervical sympathectomy; careful observation failed to reveal any difference in time of onset or depth of colour on the two sides in these cases. In patients with a facial palsy, two exhibited no difference in blushing on the two sides, two had a greater depth of colour on the healthy side, and one case previous to the test had a general flush noticeable on the palsied side.

Blushing therefore appears to be independent of the integrity of the fifth nerve and sympathetic. Observations in cases of facial palsy are as yet too few to warrant any conclusion, and this work is being carried further by a series of pharmacological and thermometrical experiments.

Accessory pathways of pain.—Recent medical literature contains frequent references to the possibility of other pathways for pain than the trigeminal nerve from the region of the face. Davis [10] in experimental work on cats suggested that the seventh nerve may subserve pain and offered clinical evidence in favour of his conclusions. It is possible that the responses of the cats in his experiments, in which the face area was stimulated with buried electrodes after cutting the fifth nerve, may have been due to proprioceptive sensation and not necessarily

to pain. Our investigations, as recorded in previous paragraphs, do not lend support to the suggestion that the seventh nerve carries impulses of pain from the face. More recently the sympathetic system has been suggested as a pathway by which pain may reach the central nervous system. The evidence offered by Foerster, Altenburger and Kroll [13] is not convincing. Frazier and Helson [15] observed the presence of the appreciation of painful hot stimuli in cases where there was anæsthesia over the maxillary and mandibular distribution, but its absence when the superior cervical ganglion had been removed as well. Since in these cases there had been only a partial resection of the central root, the observations do not prove that the inability to appreciate the hot stimuli was due to the sympathectomy.

In five cases in which the cervical sympathetic had been severed by operation for the removal of the stellate ganglion or by accidental severance of the cervical sympathetic trunk, we have been unable to obtain any difference in testing the two sides of the face by means of graded stimuli for superficial pain and deep pressure pain. Such observations are in accord with the experimental work of Davis and Pollock [9], and the conclusions of Langley [23], and the investigations of Ranson and Billingsley [26] and Cleveland [6]. These few observations, along with the experimental work quoted above, confirm our belief in Langley's contention that the cervical sympathetic is an efferent mechanism only.

The oculo-motor nerves are also a possible route by which painful sensations from the orbital region may reach the brain. That they contain afferent fibres has been demonstrated in animals by Sherrington and Tozer [27] and Woollard [31]. Following a complete destruction of the Gasserian ganglion in man, Davies [8] records a case in which the eye on the anæsthetic side was extirpated without further anæsthetization; we had a similar case. Again, pressure over the eyeball on the anæsthetic side fails to arouse pain. Diplopia never resulted from destruction of the fifth nerve in our cases; accurate fusion of the visual images may be regarded as an extremely delicate test of co-ordination of the eye musculature. On these facts one may state that the afferents in the oculo-motor nerves do not subserve pain but are probably concerned with afferent impulses requisite for accurate co-ordination of eye movements—in other words, the oculo-motor nerves do not serve as an accessory pathway for pain.

Our observations fail to demonstrate the presence of a pain pathway in the oculo-motor nerve, the facial nerve, and the sympathetic. The

trigeminal nerve thus remains the nerve for all painful impulses from the face region.

Summary.

(1) The fifth nerve is the general cutaneous nerve of the head region; the ophthalmic, formerly a separate nerve, is the most rostral of the body.

(2) In ten cases of injection of the Gasserian ganglion there was complete destruction of the ganglion as judged by the extent and completeness of the anæsthesia. The longest duration of the anæsthesia was ten years.

(3) Evidence is produced to strengthen the idea that all reflexes dependent on the ophthalmic division require a stimulus which in normal subjects is felt as pain.

(4) The problem why a number of patients after destruction of the Gasserian ganglion lose taste on the anterior two-thirds of the same side of the tongue is discussed.

(5) Evidence is presented to show that deep pressure pain depends on the integrity of the fifth nerve only.

(6) The conclusion is drawn that the afferent fibres in the seventh, other than taste, and in the third nerve, subserve a proprioceptive function and do not convey pain impulses.

(7) Blocking of the seventh nerve has no influence on the paræsthesia following destruction of the Gasserian ganglion.

(8) Throughout the investigations no evidence was obtained that impulses subserving pain in the face and orbit follow any pathway other than in the fifth nerve.

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THE LOCALIZATION OF THE PATHS SUBSERVING MICTURITION IN THE SPINAL CORD OF THE CAT.

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I.—HISTORY.

BUDGE (1864) stated that, after removal of the dorsal half of the cord at the level of the fifth cervical vertebra in a newly born bitch, stimulation of the remaining ventral half evoked movement of the bladder, rectum and tubes. He describes one experiment only.

Mosso and Pellacani (1882) showed that division of rather more than the ventral half of the cord in the posterior thoracic or anterior lumbar region of the dog did not abolish the contraction of the bladder evoked by pressure on the fore limbs, whereas division of the dorsal half did; they concluded that the motor fibres for the bladder pass by the dorsal columns or by the dorsal part of the lateral columns.

Stewart (1899) made experiments on cats. He found that when the pelvic nerve and the lumbar splanchnic nerves on the same side were divided and a hemisection of the cord made in the posterior thoracic region, stimulation of the cord in front of the hemisection produced contraction of the bladder whether the hemisection had been made on the same side as the divided nerves or on the opposite side. He concluded that there must be a partial crossing of the efferent fibres behind the level of the hemisection. In order to determine the most posterior limit of this crossing, he divided the nerves on one side, made a hemisection on the other and stimulated the cord in front of the hemisection: he then divided the cord in the median sagittal plane backwards from the hemisection, in stages, until stimulation ceased to produce a bladder contraction though stimulation behind the hemisection on the same side still remained effective. The level determined in this way was that of the most posterior strands of the fifth lumbar root. By splitting the cord in the same way but from behind forwards the anterior limit of the crossing was found to be just behind the origin of the second lumbar root. The limits of the crossing were the same for impulses passing by the sympathetic as for those passing by the sacral nerves.

By making a hemisection at the first cervical root and another on the opposite side at the twelfth thoracic and stimulating in front of the first, he showed that there was no crossing between these two levels. He found that stimulation of the cord in front of a complete hemisection on one side and a cut involving all the cord except the dorsal column on the other, anterior to the level of the second lumbar root, was ineffective in producing a bladder contraction. Stimulation in front of a hemisection on one side and a cut involving the ventral half of the cord on the other, was effective in giving rise to a bladder contraction as it was also when the middle third (dorsal and ventral columns) of the remaining side had been divided instead of its ventral half. On dissecting the dorsal half of the lateral column free from the rest of the cord and stimulating it, contractions of the bladder occurred. Division of the lateral column at the fifth and sixth lumbar roots abolished the contraction of the bladder produced by stimulating the cord in the dorsal region after the lumbar nerves to the bladder had been cut, but division of the middle third of the cord did not. Stewart therefore concluded that impulses pass down the cord to the bladder in the dorsal part of the lateral columns.

Spiegel and Macpherson (1925) experimented on decerebrate cats. They produced contractions of the bladder by stimulation of the cerebral peduncles and noticed the effect on this of lesions in the anterior thoracic region of the cord. Destruction of the dorsal and ventral columns and of the grey matter and of Lissauer's zone did not abolish the contractions, but destruction of the lateral columns did. A hemisection in the cervical region with one on the opposite side in the posterior thoracic region abolished contraction.

II.—Methods.

In all the experiments referred to in the previous section it is only the centrifugal path which is demonstrated. Impulses, produced artificially, passing from the cord to the bladder are shown equally whether they in fact occur in micturition or whether they do not: for instance, Stewart demonstrated impulses passing to the bladder by the sympathetic, but as it is known that the sympathetic supply to the bladder can be cut without producing any defect in micturition, it is open to question if such impulses take place during micturition. In none of the experiments were the animals kept a sufficient time for the partly damaged parts of the cord to recover; there must therefore have been a

loss of function during the experiments of a greater part of the cord than that actually found destroyed at the post-mortem examination.

To obviate these objections lesions were made in the cord, the cat kept alive, and the presence or absence of any defect of micturition noticed. Female cats were used in most cases. A defect might therefore be due to the destruction of the centrifugal or of the centripetal path, or of both. Two principal defects were found, the presence of residual urine and loss of consciousness of the need to micturate: residual urine, in some experiments, occurred by itself, but loss of consciousness of the need to micturate was never observed as a result of a lesion of the spinal cord in the absence of residual urine. The existence of residual urine was determined by feeling the bladder a short time after the cat had been known to have passed urine. In this way the volume of residual urine can be roughly estimated; when it was necessary to estimate the residual urine with accuracy the bladder was emptied by expression over a vessel. An intact cat at liberty in a room, on the floor of which is one of the trays of sawdust on which the cages habitually stand, will always micturate on this tray; cats who passed urine indiscriminately on different parts of the floor were assumed to have lost the consciousness of a desire to micturate.

This method is open to the objection that a part of one or both paths may be destroyed without producing an objective defect in micturition, and conversely that what appears to be a complete abolition of micturation may result when some part of the specific region of the cord is still intact. This objection can be overcome by making several experiments in the same level of the cord.

For making the lesion, the cat was anæsthetized with chloroform and the anæsthetic then changed to ether. The appropriate vertebral lamina was removed and the dura opened. The lesion was generally made either with an electro-cautery needle, or with a needle which was made the cathode of an electrolytic circuit, an indifferent anode being placed on a hind limb; these methods were found better than mechanical ways of making the lesion. The extent of the lesion was determined after killing the cat with chloroform, tying a cannula into the aorta and washing the vessels through first with warm, normal salt solution and then with 10 per cent. formalin. The part of the cord concerned was removed, embedded in paraffin, sections 10μ thick cut and mounted at each quarter of a millimetre and stained with Ehrlich's hæmatoxylin and eosin.

Lesions of the cord made in this way often, if not always, temporarily

abolish the function of some part of the spinal cord not actually destroyed, presumably by interference with its circulation. When an experiment is made for the purpose of determining localization it therefore becomes a matter of first importance to know how long a defect in function produced in this way can last, otherwise such a defect may be wrongly attributed to the absence of function of the destroyed part of the cord. The following accounts are those of two of the three experiments in which the period of recovery from a defect in micturition following operation on the spinal cord were the longest observed. The third experiment is described at the end of Section 5, and its period of recovery was intermediate between the two following :—

Experiment 1.—A lesion was made in the third lumbar segment with an electro-cautery needle, the dura having been opened on the left side. At the post-mortem examination the destroyed part of the cord on the left side was found to be the grey matter, except the tip of the ventral horn, the lateral column except a small part of it adjacent to the ventral column, and the dorsal column, except a small part adjacent to the central grey matter. The central grey matter was destroyed on both sides, but otherwise there was no destruction of the right side of the cord.

On the sixth day after the operation, there having been no voluntary movements of either hind limb, the cat had become soaked with urine. Chloroform was given, 160 c.c. of urine was obtained by expressing the bladder and rather less than that quantity left in.

On the eighth day he was again soaked with urine. Seventy c.c. of urine were expressed from the bladder and about the same volume left in. On scratching the back of one pinna there was no movement of the homolateral hind limb on either side.

On the thirteenth day he was soaked with urine. The urethral resistance was felt to be marked on attempting to express the bladder. Chloroform was given and the bladder nearly emptied by expression, 145 c.c. of urine being obtained. On scratching the back of the right pinna there was flexion of the right hip.

On the fifteenth day the cat was again wet and he dripped urine when picked up. Chloroform was given, the bladder nearly emptied by expression and 85 c.c. obtained.

On the nineteenth day he was wet. Expression of the bladder was begun. After the stream had started it continued spontaneously after removal of the pressure, but some residual urine was left, this was subsequently expressed. He could make walking movements with the right hind limb in progression if the pelvis was raised by holding the tail up.

On the twentieth day the bladder was found to contain about 20 c.c. and to be very hard ; urine escaped directly it was compressed.

On the twenty-sixth day he could walk on three legs dragging the left hind

limb after him. When 15 c.c. of urine had been passed within the previous 1¼ hours the bladder felt to contain 30 c.c.; feeling it led to the escape of urine in a continuous stream which continued after the pressure was removed. The stream stopped before the bladder was empty and about 15 c.c. were left in, which were expressed.

On the thirtieth day he made walking movements with the left hind limb.

On the thirty-first day he passed urine at least three times, from 10 to 25 c.c. being passed each time. When 15 c.c. had been passed within the previous half-hour the bladder was completely emptied by expression and 10 c.c. of residual urine obtained.

On the forty-ninth day he probably only passed urine twice and certainly passed 35 c.c. at one micturition.

On the fifty-seventh day, when he was loose in the room, he was seen to pass urine on a tray of sawdust, provided for the purpose, on two occasions, the bladder not being palpable after. This was seen again with the same result next day.

On the sixtieth day he showed stiffness in movement of the left hind leg in walking which, when he hurried, at times adducted and let his pelvis down on the left side.

The residual urine, therefore, persisted until the thirty-first day, and had disappeared by the fifty-seventh. The cat passed from the stage of retention with overflow to normal micturition through a stage of frequency of micturition with a diminishing volume of residual urine. The frequency was greater than could be accounted for by the residual urine.

Experiment 2 (fig. 6).—A lesion was made in the first lumbar segment with an electrocautery needle, the dura having been opened on either side. At the post-mortem examination the destroyed part of the cord on the right side was found to be periphery of the dorsal part of the lateral column for rather more than half its extent except for a thin strip touching the dorsal root; the lateral column was destroyed for rather more than half its thickness at the dorsal side, but the lesion tapered to a point ventrally. On the left side the destroyed part occupied the periphery of the lateral column for about its dorsal fourth; the maximum thickness of the destroyed part was rather less than a quarter of the lateral column.

On the first day after the operation the cat could walk, but frequently put the dorsa of the right hind toes on the ground.

On the third day urine was passed for the first time: within two hours of passing 5 c.c. the bladder felt as if it contained 100 c.c.

On the forty-ninth day within half an hour of passing 30 c.c. the bladder felt as if it contained 20 c.c.

On the sixtieth day she was seen to pass 55 c.c. Chloroform was given immediately after and the bladder emptied by expression of 25 c.c.

On the sixty-fourth day, 75 c.c. having been passed within the previous quarter of an hour, the bladder could not be felt. This was the first occasion on which this had occurred since the operation.

On the seventy-first day, 40 c.c. having been passed within the previous half hour, the bladder felt as if it contained 25 c.c.

On the eightieth day, 55 c.c. having been passed within the previous fifteen minutes, the bladder felt as if it contained 20 c.c.

On the hundredth day, immediately after passing 75 c.c., the bladder could not be felt.

Subsequently observations were made on numerous occasions and no residual urine detected. When at liberty she passed urine on a tray of sawdust. She was killed on the 157th day.

In this experiment, therefore, there was retention of urine with overflow. A small volume of residual urine was subsequently present, constantly up to the sixty-fourth day and intermittently up to the eightieth; after the hundredth it was constantly absent.

It is, therefore, improbable that a transitory defect in micturition due to a lesion of the cord will last more than eight weeks, but it certainly may last more than eleven and possibly even fourteen weeks. It follows that when a defect occurs conclusions with regard to localization cannot be drawn from experiments done for observations on degeneration by the Marchi method, since in this case the cat must be killed within three weeks.

III.—The Level of the Anterior End of the Deep Origin of the Efferent Fibres of the Pelvic Nerve.

Elliott (1907) made spinal transections in the posterior lumbar and anterior sacral regions and later examined the pelvic nerves for degenerated fibres. As a result of four experiments he concluded that no motor cells of the pelvic nerve are situated in front of the spinal root origin of the great sciatic nerve.

Before repeating these experiments seven experiments were made to find the most favourable period after the lesion for finding degenerated fibres. The sacral spinal roots were divided or excised on one or both sides and the cats killed after a variable number of days. The pelvic nerves were put into 1 per cent. osmic acid directly after death and left there from twelve to twenty-four hours. After prolonged washing a small piece was put into 40 per cent. methyl alcohol and left there for two or more days. It was teased in 40 per cent. methyl alcohol, treated with 30 per cent. ethyl alcohol followed by ascending strengths up to absolute and mounted in Gurr's medium. One cat was killed in three days, one in five days, and the remaining five in eight to thirteen days. In three days there was no visible change, in five days there was well-marked breaking up of the myelin into globules, but these stained little

if at all darker than normal myelin; in the remaining five cats the changes were greater the longer the period. It appeared, however, that eight days was the best period for the purpose, since the black fat droplets were so far apart after longer periods that if only a few degenerated fibres were present, it might be possible to overlook the fact that they were nerve fibres.

Seven transections were made, the cats killed in eight days and the nerves examined for degenerated fibres. The results are shown in the table:—

TABLE.

Spinal segments involved in the transection	Sacral roots from which the pelvic nerves were found to arise by dissection	Degenerated fibres
4th and 5th lumbar	1 and 2	Absent
Posterior part of 5th lumbar	1 and 2	Absent
6th lumbar	2 and 3	Absent
6th lumbar	2 and 3	Numerous
6th lumbar	1 and 2	Few
6th lumbar	1 and 2	Numerous
1st sacral	1 and 2	Numerous

The pelvic nerve in the cat commonly arises from all three sacral roots (Sherrington, 1892) (Langley and Anderson, 1895). In the experiments just described the cats were dissected after the vessels had been washed through with formalin. It seems probable that the third root, which is very fine, was ruptured in consequence of the fragility produced by the formalin and so overlooked. It appears safe, however, to infer that the two roots given were the two larger.

No conclusions can be drawn from experiments in which degenerated fibres were present, since softening extends forward and backwards from the plane of the transection for a variable and unknown distance. Softening backwards from the transection was noted as being extensive in the fourth and in the sixth experiment. It follows from these experiments that there may be two, but there cannot be three, complete spinal segments intervening between the segment from which the more anterior of the two larger roots of the pelvic nerve arises and that which contains the most anterior part of the deep origin of its efferent fibres.

A lesion better defined than a transection can be made by inserting a needle through the dorsal columns and making it the cathode of an electrolytic circuit. Four experiments were made in this way, the cats killed in eight to ten days and the destruction of the grey matter

confirmed and the limit of the lesion determined by microscopical examination. In the first and second the lesion was in the 6th lumbar segment; the pelvic nerves arose from the second and third sacral roots in one and the first and second in the other and no degenerated fibres were found in them. In the third the lesion was in the last lumbar and first sacral segments: the pelvic nerves arose by a large branch from the second sacral, one nearly as large from the third and a very fine branch from the first sacral: one pelvic nerve contained one degenerated fibre and the other none, the single degenerated fibre was one of the thickest that occur in the nerve and therefore probably afferent. In the fourth the lesion was in the seventh lumbar and first sacral segments, the pelvic nerves arose from the second and first sacral segments, six degenerated fibres were found on one side and two on the other: the teasing was not very efficient in this experiment and it is possible more degenerated fibres were present, but not more than twice the number stated. It appears, therefore, that no efferent fibres of the pelvic nerve arise as far forward as one clear segment in front of the more anterior segment from which the two larger roots of the pelvic nerve arise. In none of the three experiments mentioned was there any diminution in the urethral resistance as far as could be felt from squeezing the bladder, showing that at least the chief part of the nucleus of the dorsal nerve must have been behind the lesion in all experiments.

IV.—The Anterior Lumbar Region.

For the purpose of this paper the anterior lumbar region of the cord means the last, or thirteenth, thoracic, and the first two lumbar segments. It is the part of the cord from which the first three pairs of roots immediately behind the ribs arise, and, in most cats, the part immediately in front of the origin of the most anterior of the efferent fibres to the bladder, though in a certain proportion the second lumbar root gives a branch to the sympathetic supply of the bladder (Sherrington, 1892) (Langley and Anderson, 1895).

The extent of the part of the cord destroyed at this level in each of fifteen cats is shown as a dotted area in figs. 1 to 15. The segment involved, and in cases where a permanent defect in micturition followed the operation, the number of weeks after the operation for which observations were made are also shown. In the case of Nos. 1 to 4 the cats had both residual urine and loss of consciousness of the need to micturate as long as observations were made. In Nos. 5 to 9 neither of

these defects were present when the cat was killed. In Nos. 10 to 15 residual urine was present as long as observations were made, but there was no permanent loss of consciousness of the need to micturate.

If a lesion such as those in Nos. 1 to 4 is unilateral the cat carries the tip of the tail deflected towards the side of the lesion. When the movements of the homolateral hind limb are affected the most frequent condition is that the dorsa of the toes are dragged on the ground in bringing forward the limb for walking; if the affection is greater the dorsa of the toes are stood on when the body is moving forwards on this limb. The affected limb may remain stiff and rather slow in its movements. When the lesion is bilateral the tail is often arched over the back instead of pointed straight up when the cat is pleased: in No. 1 this was so marked that the tip touched the back in the region of the scapulæ.

The effect on micturition of bilateral lesions of the position and extent as those in Nos. 1 to 4 is that retention of urine occurs and progresses to overflow. Hæmaturia, sufficient for the blood to be visible to the naked eye, is not uncommon at this stage. The cat is continually soaked with urine and shows no sign of pain even if the bladder is squeezed. After a period, which may be only three days and is never more than two weeks, urine is passed in jets at intervals. The appearance at this stage is associated with a diminution in the volume of residual urine and in the urethral resistance which can be felt if the bladder is squeezed. The volume of urine passed at micturition in normal cats has great individual variations. In seven experiments the volumes of urine passed at micturition were observed before the operation: the volume of residual urine after the operation and after the passage of urine in jets had become established was about the same as that passed at micturition in two of these and less in five. If, as in Nos. 1 to 4, the lesions are not extensive enough to seriously affect the cat's movements, jets of urine are usually passed while the cat is walking about. Each time a jet passes there is a momentary pause in walking with a slight lowering of the pelvis or movement of the base of the tail, or both together. The cat appears quite unconscious of passing urine and makes no attempt to bury it unless it accidentally comes across the puddle in the course of its further wanderings. Pleasure and anger both seem to lead to the passage of jets of urine. Jets can be evoked by scratching the cat's head or stroking its back, and they occur when it is evincing pleasure for no apparent reason either by rubbing its sides against vertically situated objects or by

kneading with its fore paws; they also occur if the cat has seized a piece of meat and is growling at the approach of another cat. The passage of a jet is not immediately produced by a straining movement such as jumping. The cats never select places on which to pass urine. Though the amount passed in each jet is small, probably more often 2 c.c. than 5 c.c., a considerable volume of urine may be passed in a short period because numbers of jets occur at short intervals. Urine is either not at all, or only rarely, passed during sleep. For these reasons a considerable volume of urine is usually passed within a short period after work has started in the animal house in the morning. Cats with such lesions may be soiled with urine and fæces round the perineal region, but this is not usually the case. If cystitis supervenes from a naturally occurring infection the residual urine diminishes almost to nothing and the perineal region becomes soiled with urine owing to its passage becoming nearly continuous.

No. 4 was conscious of needing to defecate, but its sensations in this respect were imperfect, for though he would squat on the sawdust tray defecation would not take place until after he had got up and was going away. No notes were made on defecation in Nos. 1, 2 and 3, but in another cat, whose lesions are not figured, there was certainly no consciousness of wanting to defecate since she would do this anywhere: the smaller of the two lesions in this cat was in the position of those in No. 4, but extended slightly deeper into the cord.

In three cats with such lesions, including Nos. 1 and 3, and in two others having the inferior mesenteric ganglia excised in addition, a spinal transection was made in front of the lesion in the ninth, tenth or eleventh thoracic segment. In one of these one observation only was made on the twelfth day after the transection and the residual urine was found to have increased from 65 to 80 c.c. before the transection to 200 c.c. after. The remaining four were each observed on three to eight occasions after the transection. On one occasion in each the volume of the residual urine showed a marked increase over that present before the transection, but on all the other occasions it was approximately the same after as before the transection. It therefore appears that after the transection the volume of the residual urine may, on occasions, be considerably greater than before it, but that at most times it is about the same. It seems probable that the occasional increase arises from the diminished activity of the cat resulting from the transection producing a diminution in the frequency with which the passage of jets of urine is reflexly evoked. In four of the five cats it

was noted that in the early days after the transection the urethral resistance, felt on squeezing the bladder, was low, as it had been before the transection: had the transection been made in a previously intact cat the urethral resistance at this stage would have been high. The fifth cat was exceptional in that the palpable urethral resistance was considerable both before and after the transection.

If the inferior mesenteric ganglia are excised at the same time as a lesion such as those in Nos. 1 to 4 is made no obvious difference in the course of events described occurs. The inferior mesenteric ganglia were excised in three cats in which the lesions had been made from fifty to one hundred and eight days previously, one being No. 2 sixty days after the lesions had been made: in one a slight, and in two a marked, diminution in the residual urine followed.

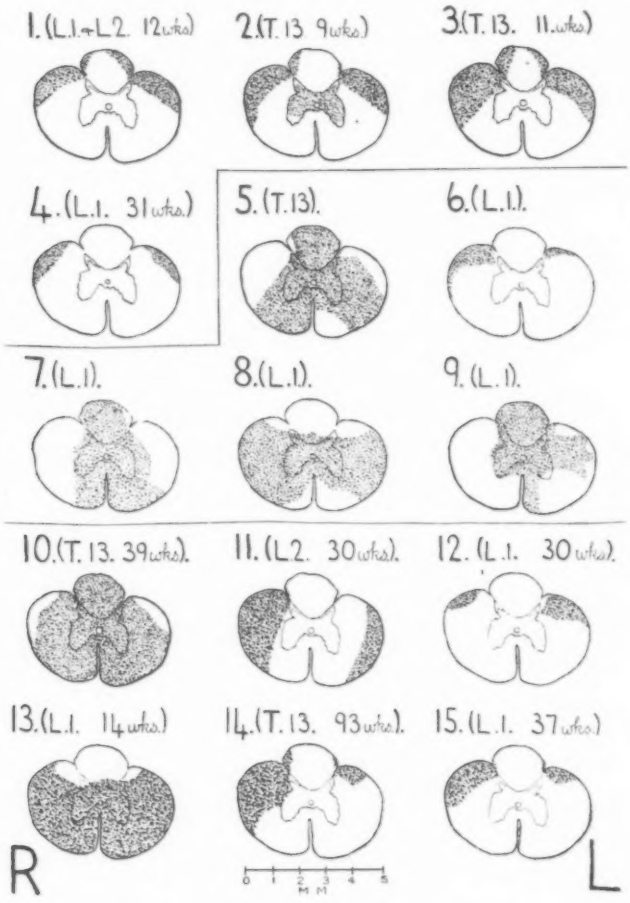
If the pudic nerves are divided after a lesion, as those in Nos. 1 to 4, has been made and the urine has come to be passed in jets, the passage of urine in jets ceases and the urine runs away in drops which are faster during straining movements; if previously clean, the perineal region becomes dirty and movements associated with passing jets, such as lowering of the pelvis and depression of the base of the tail, do not occur.

In one cat lesions were made in the position described and the inferior mesenteric ganglia excised; in ninety-five days the pelvic nerves were divided. This was followed by a great increase in the residual urine and in the urethral resistance, felt on squeezing the bladder. In four other experiments the pelvic nerves, dorsal sacral spinal roots or one on one side and the other on the remaining, were divided at the time of making the lesions or before. The urethral resistance remained high for ten to thirty-three days, and when it did diminish cystitis was present.

The effect of division of each of the three pairs of nerves on the condition resulting from these lesions is therefore exactly the same as the effect on the condition which follows a complete transection (Barrington, 1931). It may therefore be concluded that all the effects on micturition which follow a complete transection of the cord are due to the destruction of a small part of it and that this part has been largely or completely destroyed in each of the cats Nos. 1 to 4. This conclusion is supported by the fact that the condition resulting from the lesions, as far as micturition is concerned, does not differ from that resulting from a spinal transection.

When the positions of the lesions in Nos. 1 to 15 are used for the

purpose of localizing the micturition paths it must be remembered that since a unilateral lesion, however extensive, causes no defect in micturition the whole or a large fraction of the paths must have been destroyed on both sides in experiments in which a permanent defect in



micturition results, whereas the paths may have been spared on only one side in experiments in which no such permanent defect results.

The only part of the cord destroyed on both sides in each of Nos. 1 to 4 is that destroyed on the left side of No. 4, namely, a part of the dorsal half of the lateral column extending from the periphery inwards

for one-fourth or less of the thickness of the column, nearly reaching the dorsal root dorsally and to the middle of the periphery of the column ventrally. The whole or a large part of either the centrifugal or centripetal path or of both must therefore be in this part of the cord. Nos. 5 to 9 show that no large part of either path can be in any region of the cord except in the dorsal half of the lateral column, since in one or other of them all other parts are destroyed on both sides. The only point in localization left to consider is whether either path is situated in any other part of the dorsal half of the lateral column than that just described.

In No. 10 the destroyed and undestroyed parts are nearly the reverse of those in No. 4. If, therefore, the whole of both paths are in the part of the cord destroyed in No. 4, No. 10 should have had no permanent defect in micturition.

No. 10 was a castrated male. Retention of urine followed the operation and overflow occurred on the third day after the operation. He was then given chloroform and the bladder emptied by expression to 220 c.c. of residual urine. Overflow recurred on the fifth day, when expression of the bladder under chloroform gave 90 c.c. of residual urine. On the sixth day, within an hour and a quarter of passing 20 c.c., the bladder felt as if it contained 10 c.c. Up to the thirteenth day he continued passing small volumes at a time, and whenever the bladder was felt he seemed to have a volume of residual urine varying from 10 to 40 c.c. By the twentieth day he was passing larger volumes of urine at a time, and on that day, for the first time, no residual urine could be felt after he had passed 45 c.c. From then onwards until the last observation, on the two hundred and sixty-sixth day, residual urine was sometimes absent, but more often present, though the volume was usually only about 10 to 15 c.c.: the volume of urine passed at each micturition increased slightly after the twentieth day. Following the operation, the hind limbs were kept flexed at the hips and fully extended at the knees and ankles, they were rigid and not used in progression. On the nineteenth day it was found that, if his pelvis was supported by holding up the tail, he made appropriate movements with the hind limbs on walking, better with the right limb than with the left. On the sixty-third day he could stand on all four limbs, but could not walk with the hind ones. On the seventy-eighth day he was brought down to the working room, where he remained until the hundred and eighteenth. During this period he passed urine and fæces wherever he happened to be sitting or lying, and never made any attempt to get

to the sawdust tray or any other special place. He never, however, made any attempt to move his position except when he heard the attendant bringing his food; if he were then in his cage with the lid open, he would climb out actively, using the fore-limbs only; the side of the cage was 36 cm. high. He licked himself all over, including the paralysed hind limbs. On the two hundred and twenty-third day he could get up on all four limbs, but when he started to move the hind limbs let the pelvis down, because they moved too slowly to correspond with the movements of the fore limbs. He was again brought down to the working room on the two hundred and thirty-ninth day and kept there until he was killed. He was seen to pass urine in the squatting position as other cats do. When he passed urine or fæces outside his cage, he did it on the sawdust tray. It seems that the persistent presence of a small volume of residual urine intermittently must be attributed to destruction of part of a micturition path, and not to an indirect effect arising from the affection of his skeletal muscles, since micturition did not appear affected by this, and since such a defect did occur in other experiments when there was no impairment of locomotion.

As the comparisons of Nos. 10 and 4 leave some doubt about the extent of the paths, the extent of the centrifugal path in the anterior lumbar region was investigated by the old method of observing what lesions in this region abolished the contraction produced by stimulation of the cord in front of it. In four cats lesions were made in the anterior lumbar region sixteen to twenty weeks before the final experiment. All four had persistent residual urine and persistent loss of consciousness of the need to micturate. The hypogastric nerves were divided and the cord transected in the eighth to eleventh thoracic segment under chloroform: decerebration was performed and the chloroform stopped. A wide opening was made in the left side of the abdomen and the bladder observed directly. In two cases contraction occurred with stimulation and in two it did not.

The extent of the smaller lesion in the first two were respectively:—

(1) The periphery of the dorsal half of the lateral column not quite reaching the dorsal root and extending into the column for rather more than a quarter of its thickness, and

(2) The periphery of the dorsal half of the lateral column reaching the dorsal root and extending inwards for less than a quarter of its thickness.

The extent of the smaller lesions in the second two were respectively:—

(1) The dorsal half of the periphery of the lateral column not quite reaching the dorsal root and extending inwards for about a third of its thickness.

(2) The dorsal half of the periphery of the lateral column reaching the dorsal root and extending inwards for about a third of its thickness.

The position and extent of the centrifugal path in the anterior lumbar region is therefore the periphery of the dorsal part of the lateral column, except a small part touching the dorsal root, and it extends inwards for about a third of its thickness. The deep part of this region was not destroyed in No. 4 and was destroyed in No. 10. No. 10 shows that no considerable part of the centripetal path can exist in any other part of the cord since the micturition defect it exhibited was so slight.

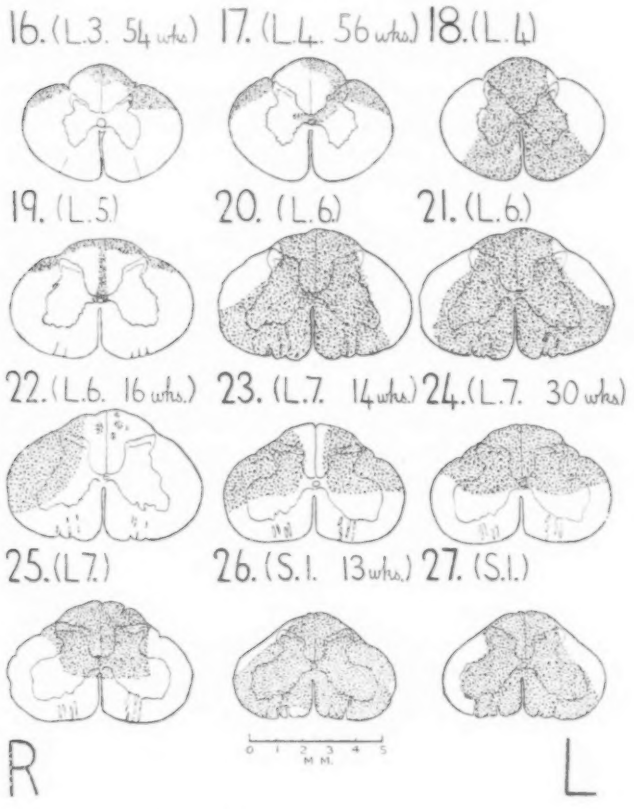
Nos. 5 to 9 had no permanent defect in micturition, and of these Nos. 5, 7 and 9 had no defect at all. No. 6 has been fully described in Section 2, and No. 8 had residual urine up to the 18th to the 27th day. Hence the only two of the five that had residual urine which disappeared were the only two that had part of the periphery of the dorsal half of the lateral column destroyed on both sides.

No. 10 has already been described. No. 11 had retention with overflow followed by the presence of residual urine which disappeared as far as could be felt on the thirty-sixth day. When killed, half an hour after micturition, 15 c.c. of urine were present in the bladder although this had not been felt before. He was very fat, so it is possible that a small volume of residual urine was repeatedly overlooked. He was conscious of wanting to micturate but not of micturating, since he would pass urine on the sawdust tray sometimes while standing on it before he had begun to scratch the sawdust, sometimes while still standing and actually scratching the sawdust and sometimes when standing just after he had squatted but passed no urine. His consciousness of a need to defecate was more defective still since faeces was usually passed in an unselected place and not on the tray. The remaining four cats had greater defects in micturition corresponding to the greater part of the periphery of the dorsal half of the lateral column destroyed on either side. They all had retention with overflow followed by the persistence of residual urine, which was very small in amount in No. 15, and they all either retained or recovered the consciousness of needing to micturate. No. 13 was probably unconscious of needing to defecate, and No. 14 was certainly conscious of it. The experiments

in which incomplete defects in micturition occurred therefore confirm the supposition that both the centrifugal and the centripetal paths are situated in the part of the dorsal half of the lateral column extending inwards for a third of its thickness. The dorsal portion of this part of the cord is peripheral to the crossed pyramidal tract.

V.—The Posterior Lumbar Region.

Figures 16 to 27 show the position of lesions behind the second lumbar segment in each of twelve cats. Lesions in the sacral region,



particularly posteriorly, which are followed by micturition defects are of little use in localization since there is no adequate method of controlling the integrity of the sacral spinal roots after the lapse of months and the

probability of their injury affecting micturition increases from before backwards.

No. 16 was a castrated male. A large volume of residual urine persisted, and as long as he lived he was unconscious of needing to micturate and of micturating. He commonly passed urine in jets, but besides this, at times, considerable volumes would be passed in a long stream. Sometimes through the abdominal wall the bladder could be felt to harden and a further considerable volume of urine was then passed. The last two facts seem to show that the destruction of the micturition paths was incomplete, and this corresponds with the destroyed part of the cord involving less than the dorsal half of the periphery of the lateral column. His anus was patulous and often fæces could be seen within it for hours before any were passed. He sometimes passed, or endeavoured to pass, fæces in selected places. This, together with the fact that he resented having pressure made on his colon through the abdominal wall though not on his bladder, shows that he preserved at least some sensation of needing to defæcate.

No. 17 had a large volume of residual urine and was unconscious of micturating and of wanting to micturate. She was clean and did not become soiled with urine or fæces. The segment involved was the third lumbar and not the fourth; it has been recorded as the fourth, as fourteen thoracic segments were present instead of thirteen, together with the usual number of eight cervical segments.

No. 18 had no residual urine. No steps were taken to find whether or not he was conscious of needing to micturate.

No. 19 had residual urine for three weeks but not after four weeks. No steps were taken to see whether or not she was conscious of wanting to micturate.

No. 20 had no residual urine. It was not known whether she was conscious of needing to micturate.

No. 21 had no residual urine and was conscious of needing to micturate.

No. 22 also had a lesion in the last thoracic segment which involved the dorsal two-thirds of the left lateral column for about half its thickness from the periphery inwards and which did not quite reach the dorsal root. She had retention of urine with overflow followed by residual urine and was unconscious of wanting to micturate.

No. 23 had residual urine and was unconscious of the need to micturate.

No. 24 had residual urine, but knew both when she wanted to micturate and when she was micturating.

No. 25 had retention of urine with overflow: residual urine followed but its volume was very small after the first two weeks and it was absent in seven weeks. She retained, or more probably recovered, consciousness of the need to micturate. She occasionally lost a few drops of urine while walking about.

In No. 26 the anterior end of the lesion was in the seventh lumbar segment and the destruction of the grey matter extended antero-posteriorly for about six millimetres, so it is unlikely that it extended into the second sacral segment. The pelvic nerves were found by dissection to arise by a large branch from the second and a small one each from the first and the third sacral roots. Retention with overflow occurred and the compressor urethræ was not paralysed, as could be felt by squeezing the bladder. Residual urine persisted. Ultimately she generally passed urine on the sawdust tray, but she sometimes used to walk about before she had finished micturating. She therefore was conscious of the need to micturate but not of micturating. At times she used to lose a little urine while sitting down.

No. 27 had no residual urine. The pelvic nerves were found by dissection to arise by a branch from the first and another from the second sacral nerves, that from the second being the larger.

The results of these twelve experiments are therefore consistent with the paths of micturition being in the same position as in the anterior lumbar region. Nos. 26 and 27 cannot be compared, since although No. 27 appears to have had the more anterior lumbo-sacral plexus the posterior limits of the lesions in the two cases were not recorded sufficiently precisely for comparison. It may be concluded that both centrifugal and centripetal paths are in the periphery of the dorsal half of the lateral columns in the third, fourth and fifth lumbar segments, that they must be within the dorsal three-quarters of the lateral columns in the sixth lumbar segment, and within the dorsal half in the seventh, and that they may still be largely in the lateral columns in the first sacral segment.

The operation of division of one pelvic nerve in the cat is not uncommonly followed by the presence of a significant volume of residual urine which can persist at any rate for several weeks. Since this result is not only not constant but does not even occur in the majority of cases, it seems probable that it is not due to division of nerve-fibres but to some other effect of the operation.

The only probable way in which residual urine might result from an unintentional lesion made at the operation is by stretching the

remaining pelvic nerve in retracting the rectum. Against this being the cause of the residual urine is the fact that signs of paralysis of these nerves do not occur in acute experiments where both nerves have been exposed in the way used in survival experiments and not divided. To whatever cause this residual urine is due its importance for the present purpose is that when it follows a combination of division of one pelvic nerve with another lesion, the possibility of its being due to division of the pelvic nerve alone must always be excluded before assuming it is due to the combination. This can be done by dividing the nerve and seeing if residual urine follows before making the other lesion.

In one cat the right pelvic nerve was divided and no residual urine followed. In eleven days a lesion was made in the first lumbar segment which destroyed the whole of the right side of the cord except a small part of the periphery of the ventral column, together with the internal and dorsal sides of the dorsal column and the central grey matter on the left side. Residual urine followed and persisted for nine days but had disappeared in twenty-one days. In a second cat the left pelvic nerve was divided and a residual urine of 5 to 10 c.c. followed, the volume passed at each micturition being usually about 50 c.c. On the nineteenth day a lesion was made in the last thoracic segment which destroyed the whole of the right side of the cord except the ventral column, together with the dorsal column, the central grey matter and the internal part of the dorsal grey horn on the left side. There was a transient increase in the volume of residual urine which disappeared between the seventh and twenty-second days. In a third cat a lesion was made in the adjacent parts of the second and third lumbar segments, destroying rather more than the dorsal half of the right lateral column for more than half its thickness from the periphery inwards. The left pelvic nerve was divided twenty days later and no residual urine followed. In a fourth cat the left pelvic nerve was divided and no residual urine followed. In fourteen days a lesion was made in the adjacent parts of the second and third lumbar segments which destroyed the lateral column, the dorsal grey horn and the external part of the ventral grey horn on the right side. Residual urine followed but had disappeared in eighteen days.

From these four experiments it follows that there is an extensive but incomplete crossing of both the centrifugal and centripetal paths between the anterior lumbar region and the origin of the pelvic nerves.

The level of this crossing can be determined by making a unilateral lesion in the anterior lumbar region involving at least the peripheral

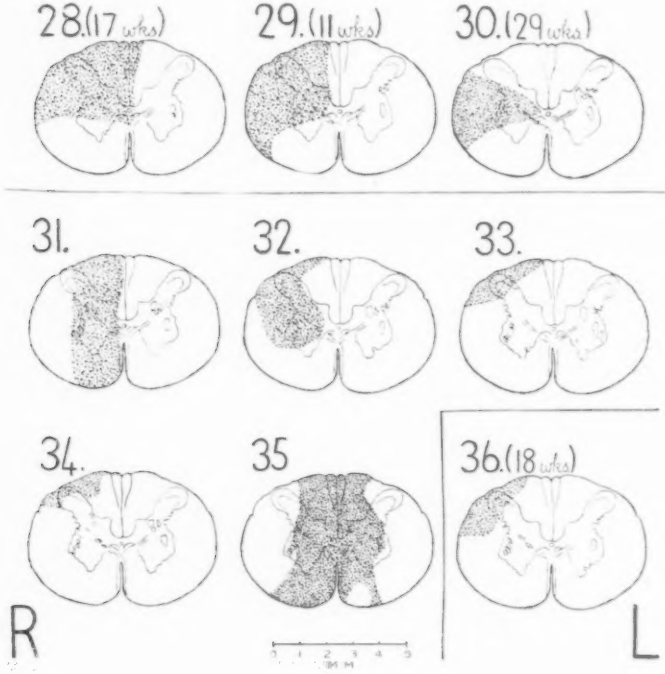
fourth of the dorsal half of the lateral column, combined with a similarly situated contralateral lesion further back, and observing how far back the latter can be made and be followed by both the defects in micturition which follow similar bilateral lesions in the anterior lumbar region. It can also be determined by dividing one pelvic nerve and subsequently making a contralateral hemisection and observing how far back the latter can be without being followed by any, or any additional, defect in micturition.

No. 22 shows that the crossing must be behind the sixth lumbar segment. The same results as those of No. 22 followed in a cat when the posterior lesion was in the seventh lumbar segment and they lasted twenty-eight weeks, when the cat was killed. In a third experiment with the same results, in which observations were made for twenty-two weeks, the posterior lesion was in both the seventh lumbar and first sacral segments, and at its maximum was a complete hemisection except for a thin strip of the ventral column along the ventral median fissure; the pelvic nerves were found by dissection to arise from the second and third sacral nerves, the branch from the second being the larger. This method therefore shows that the crossing must take place in the segments from which the pelvic nerve arises.

The same result is given by the second method. Three experiments were made, the left pelvic nerve being divided in each. In one after four weeks there was a small volume of residual urine. A lesion was then made which involved the dorsal horn, the external part of the dorsal column and the dorsal half of the lateral column on the right side in the fourth and fifth lumbar segments, without any increase in the residual urine following. In the second there was no residual urine and a lesion in the first sacral segment involving the whole right side of the cord and the central grey matter and internal part of the dorsal column on the left side was followed by residual urine which disappeared after twenty-two days. The right pelvic nerve arose by a large branch from the second sacral nerve, a smaller one from the first and a very fine one from the third. In the third experiment there was no residual urine and a lesion in the seventh lumbar segment involving the whole of the right side of the cord together with the greater part of the left dorsal column and adjacent grey matter was followed by the intermittent occurrence of a small volume of residual urine up to the sixty-second day, but not after. The right pelvic nerve arose by a large branch from the second sacral root, one about a quarter of the size from the first and a smaller one still from the third.

VI.—The Cervical and Thoracic Regions.

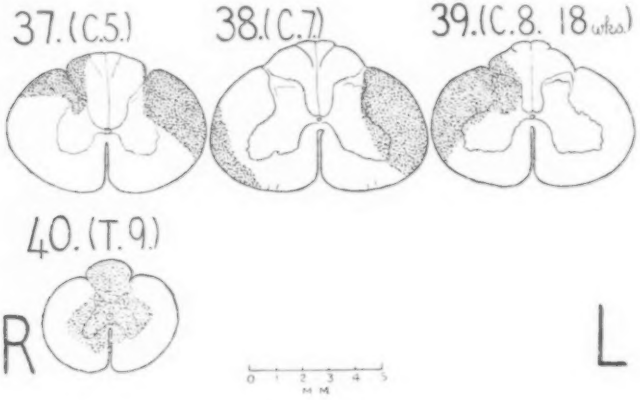
A lesion of the periphery of the dorsal half of one lateral column, which involves at least a fourth of its thickness in the anterior lumbar region, combined with a lesion in the first cervical segment on the opposite side, may result in the presence of residual urine and loss of consciousness of a need to micturate. In two cats such a lesion in the anterior lumbar region was combined with a lesion on the same side



in the first cervical segment. In one cat this lesion was a hemisection and in the other only a thin medial strip of the dorsal column, grey matter and ventral column escaped: neither cat developed residual urine. Three similar experiments were made with the same result, the anterior lesion being in the first, the sixth and the seventh thoracic segments respectively. In all three a small part of the homolateral ventral column escaped destruction, and in the case of the sixth thoracic a small medial part of the dorsal column in addition. There is therefore

no crossing of either path in the cervical or thoracic regions unless it is insufficient in degree to escape detection by the present methods.

Figs. 28 to 36 show the position and extent of lesions in the first cervical segment of each of nine cats. In each case the lesion was combined with one on the left, or contralateral, side in anterior lumbar region, or in the case of No. 36 in third lumbar segment, which involved at least the dorsal half of the lateral column for one-fourth of its thickness from the periphery. The number of weeks indicated after the number of the figure is the period for which observations were made after the second of the two operations. Nos. 28, 29 and 30 had residual urine and were unconscious of a need to micturate, Nos. 31 to 35 had



no objective defect in micturition at the time they were killed, and No. 36 constantly had a small volume of residual urine but was conscious of needing to micturate.

Attempts to make a narrow lesion involving the dorsal half of the periphery of the lateral column always resulted in the formation of a deep one, apparently by infarction. In consequence of this the three positive experiments, Nos. 28 to 30, only show that both paths must be in some part of the dorsal half of the lateral column or in the wedge-shaped area of grey matter subtended by this towards the central canal. In four out of six cats in which retention was produced by a lesion in the first cervical segment on one side followed by one in the anterior lumbar region on the other, the urethral resistance was low when overflow first occurred. In other respects the micturition defects in Nos. 28, 29 and 30 were identical with those already described resulting

from bilateral lesions in the anterior lumbar lesion, and these cats were also unconscious of needing to defæcate.

In numbers 31 to 36 retention did not occur. There was no residual urine in Nos. 31 to 35, but there was in No. 36. There was no loss of consciousness of the need to micturate in Nos. 31, 32, 35 or 36: observations on this point were not made in Nos. 33 and 34. It will be seen from the diagrams that more than the dorsal fourth of the periphery of the lateral column has to be destroyed before residual urine results, and that more than the deep half of the dorsal half of the lateral column can be destroyed without any residual urine resulting.

Nos. 37 to 40 show the position and extent of lesions in four of the remaining segments of the cord in each of four cats. In No. 39 there was also a lesion in the first lumbar segment on the left or opposite side which involved the periphery of the dorsal half of the lateral column: the cat had residual urine and was unconscious of needing to micturate. Nos. 37, 38 and 40 had no residual urine.

Conclusions.

The centrifugal and centripetal paths of micturition undergo extensive crossing in the segments from which the pelvic nerves arise and possibly in the segment next in front of these. From then forwards there is either no crossing or it is insufficient to be detected by the methods used. Both paths are situated in the dorsal half of the lateral column near its periphery.

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ON THE PHYSIOLOGY OF MICTURITION.

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(1) Introduction.

Mosso and Pellacani, in 1882, when the method of making continuous smoke-drum records had just been introduced by Marey, described a series of experiments upon the normal female human bladder [18]. Their method was highly ingenious, and consisted of running records of the movements of a vessel of which the fluid contents communicated by tube and catheter with the interior of the bladder. The level of the fluid was kept constantly slightly above the level of the bladder and the record was therefore of variations of vesical volume at constant pressure. They described and figured slow fluctuations of vesical volume occurring at times spontaneously and at times in response to attempts to micturate. They were especially concerned to eliminate change of abdominal pressure, or variation of blood-pressure as a cause of these fluctuations. The fluctuations of volume were interpreted as active vesical contractions. Similar fluctuations were found to occur when the subject exerted emotional or intellectual effort, and the function of the organ was therefore considered to be closely related to the intensity of psychological processes. Introduction of an additional volume of fluid revealed a subsequent adaptation of the bladder to its contents.

provided the immediate reaction to introduction was allowed to subside, so that the pressure within the organ gave little or no indication of the volume it contained. It was concluded that desire for micturition was stimulated when the pressure rose above 18 cm. of water, and was not directly related to volume.

Subsequent observations upon the human bladder by many authors, made by measuring at intervals the pressure of fluid by a water manometer connected to a catheter, confirmed the process of adaptation to a mean pressure which rises little as volume increases over a moderate range. Sooner or later a volume is reached at which an active vesical contraction occurs and fluid is ejected from the bladder at high pressure (Rehfisch [21], Schwarz [24], Dennig [6], Adler [1]). Records of vesical pressure obtained by this means tended to belittle and indeed disclaim any rhythmical contractile activity in the human bladder (Dennig [6]).

Rehfisch [21] observed that even if the external, voluntary sphincter were held open by a catheter the vesical contents were retained by the internal involuntary sphincter which embraces the most proximal urethra. He stated that micturition could be commenced voluntarily under these conditions and maintained, therefore, that the internal sphincter relaxed by effort of will. Boeminghaus [5], by means of X-rays of the bladder filled with opaque solution, demonstrated that the internal sphincter is normally completely closed until micturition occurs. He also observed that after prostatectomy, by methods which destroyed the internal sphincter, urine was still retained by involuntary activity of the external sphincter. Young [29] devised an instrument to dilate the internal sphincter while allowing the external sphincter opportunity to close, and found that urine could be held comfortably by the external sphincter. There is therefore some evidence that both sphincters can function involuntarily in retaining the contents of the viscus. The manner and degree of ability to relax these two sphincters and the manner in which voluntary and involuntary closure is brought about has remained in doubt.

Rehfisch [21] found, by introducing a catheter of fine calibre into the bladder and measuring vesical pressure by a manometer tube, that a large rise of pressure occurs during micturition. The relationship of this vesical contraction to the onset of micturition and the mode of transition of involuntary adaptation of the bladder to active micturition remained matters of speculation.

The extensive researches of Mosso and Pellacani [18], von Zeissl [32],

Rehfisch [21], Sherrington [26], Elliott [8], Barrington [3, 4] and others into the innervation of the bladder upon animals has been admirably reviewed by Fearnsides [9] and Barrington [3], and more recently by Dennig [6] and Adler [1]. Of the two pairs of nerves reaching the vesical plexus, the sacral (parasympathetic) nerves, derived from the sacral plexus, when stimulated relax the internal sphincter and contract the detrusor musculature of the vesical wall. The "hypogastric" nerves derived from the sympathetic chain on each side via the inferior mesenteric ganglion, have in general the reverse effect. The effect of stimulation of this nerve upon the internal sphincter and trigone in man has recently been described by Learmonth [17]. Section of the hypogastric nerves has been followed only by slight frequency of micturition, a finding which suggests more function by the remaining sacral nerve supply in regulating adaptation to volume than the effect of its stimulation would indicate. The external or voluntary sphincter, innervated by the pudic nerve, appears to have little part in the initiation or completion of micturition, but the researches of Barrington [4] reveal some slight but constant incontinence following the section of this nerve in animals. It has been stated that there is no voluntary sphincter in the female urethra and that this sphincter plays no essential part in micturition, but Zangenmeister [31] describes and pictures sufficient voluntary muscle situated around the proximal female urethra to refute this statement. Goltz [11], from observations on micturition in the spinal animal, put forward the view that spontaneous contractions of the bladder caused the expression of some drops of urine into the posterior urethra, with consequent desire for micturition and completion of the act. The series of reflexes described by Barrington [4] would appear to provide the mechanism for the completion of the process. Guyon [12], however, showed that distension or irrigation of this proximal part of the urethra in man had no demonstrable effect in facilitating micturition or in stimulating desire to micturate.

Most authors except Rehfisch [21], Adler [1] and Le Gros Clarke [16] are unwilling to allow the possibility of any direct voluntary control over the smooth muscle of the bladder and internal sphincter. Müller [19] seeks to avoid this implication by suggesting a reflex control of the bladder by afferent impulses arising in the voluntary external sphincter, and thus willed effort to micturate would affect the bladder indirectly. Schwarz [24] obtained records of vesical pressure by means of a fine catheter and manometer, and noted the relationship of the onset and termination of micturition as it

occurred around the catheter. Both Schwarz and Rehfisch maintain that a rise of vesical pressure is the primary event in voluntary micturition. Their methods, however, do not give information as to the part played by the internal sphincter in the initiation of the act. Adler [1, 2] holds that the primary event is relaxation of the internal sphincter with subsequent reflex relaxation of the external sphincter and vesical contraction. The effective performance of micturition after prostatectomy with excision of the internal sphincter and prostatic urethra seems to indicate that these structures play no very necessary part in the initiation of the act.

Considerable variation in opinion therefore exists as to the sequence of events in normal human micturition. In the course of some work on the disturbances of micturition by nervous diseases we have developed a technique for obtaining continuous records of vesical pressure during manipulations of the volume of the bladder. In the control experiments upon normal subjects we have accumulated some data bearing on the sequence of events in normal micturition and their control, and present them here, together with a description of the method we have employed.

(2) Method.

The method of recording vesical and urethral pressure which has been used has developed in the course of a study of the disturbances of micturition in twenty-five cases of nervous diseases. The present work is based upon seven prolonged experiments on three male subjects, all of whom were in perfect health, except that Subject C was a patient suffering from a chronic retinal condition. In no subject was there reason to believe that micturition was or ever had been in any way abnormal.

With aseptic precautions the subject of the experiment is catheterized with a soft rubber catheter of moderate size and having its proximal aperture situated at the tip. Through this catheter is passed an ordinary ureteric catheter of small outside diameter. No anæsthetic was used in any of the experiments. The distal extremities of the two catheters are attached to a sterile glass adapter arranged as in fig. 1 B, so that the small ureteric catheter *b* gained exit from the space connected with the lumen of the rubber catheter *a*, by a small rubber cork *d*. The ureteric catheter was led to a small glass adapter *e*, to which it was attached so that its lumen communicated with the interior of the adapter. The glass adapters each contained a pressure chamber *f* and *l*. The fluid was allowed to reach a level in each pressure chamber; on changes

of pressure in the interior of the catheters the fluid level rose or fell independently in the two pressure chambers.

The pressure within the pressure chambers was transmitted by air in thick-walled rubber tubing g and m, to the interior of two manometers, each consisting of a small glass funnel, as is shown in fig. 1 A o, over the mouth of which is stretched stout rubber sheeting p, which is fixed by wire binding at the lip of the funnel. As the rubber membrane

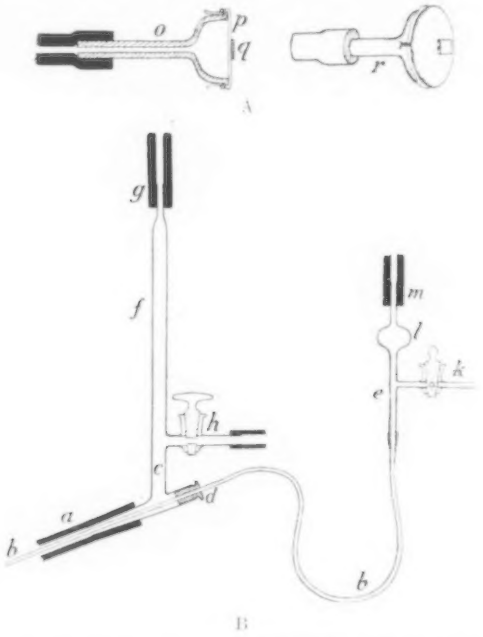


FIG. 1.—Diagrammatic section of the apparatus used to register the pressure within the catheters. Fig. 1 A shows the construction of the mirror manometer used; B shows the connections of the two catheters, a and b with the glass adapters which serve to transmit the pressure in each to the appropriate manometer. The details are explained in the text.

has to withstand pressures of over 200 cm. of water, the rubber must be of such strength that it bulges only about a millimetre at this pressure, and the joint between rubber and glass is sealed by varnish ("gold size" was found most suitable) so that the system is completely air-tight. To one side of the rubber diaphragm is attached by varnish a small mirror of polished stainless steel with an optically flat surface q. The manometers are fixed in adjustable clamps so that each may be adjusted independently, and are attached to an upright steel pillar set in a

cement floor so firmly that no ordinary movement on the floor caused in them any evidence of vibration.

Change of air pressure within the manometer, transmitted from its pressure chamber by some 60 cm. of rubber tubing, caused equivalent fluctuation of the diaphragm and consequent swinging of the steel mirror through a slight angle. A beam of light passing through a narrow slit is thrown upon the mirrors and by them reflected at an angle to fall upon the slit of a moving paper camera situated 2·2 metres from the manometers. As a continuous strip of bromide paper, 7·5 cm. in width, moves in the camera past the slit the reflected beam of light traces the fluctuations of the mirrors with high magnification. A revolving Rayleigh electrical time marker interrupts a steady beam of light on the edge of the paper so that a continuous series of fine vertical strokes are made at $\frac{1}{5}$ sec. intervals. The shadows of two electromagnetically operated signals are arranged to fall upon the camera slit and thus record their movement upon the paper. By operating a switch a movement of one or other can be made at will. Three other manometers, similar to those for the catheter pressure chambers, were used to record the movements of the abdominal wall, the pressure within the rectum, and the movements of the perineum by means of small rubber balloons attached to thick walled rubber tubing. These were moderately distended, and the abdominal and perineal balloons were placed under binders which held them applied to the umbilicus and over the M. bulbocavernosus respectively. The rectal balloon was some 3 cm. in diameter when fully distended and was introduced, well lubricated by soap, into the rectum where it was slightly inflated by introducing some air into a side tube of the manometer.

The subject lay supine upon a couch and was provided with an electrical key by which he could signal any events he wished upon the camera paper. The lower limbs were slightly flexed and abducted, and an upright supported the two glass adapters so that they were conveniently near the penis.

To each glass adapter, in the lower part of the pressure chamber, a side tube with tap (fig. 1 B *h* and *k*) is arranged, and to either can be attached a length of rubber tubing leading to a reservoir graduated in cubic centimetres and containing a thermometer. The reservoir was of moderate capacity, 600 c.c., so that it could be readily raised and lowered by hand. With the disposition of catheters shown in fig. 2 A the reservoir was connected to *h*, with that in fig. 2 B, C, D, to *k*.

The pressure at which the fluid was introduced into or removed from the bladder was measured by arranging a vertical scale graduated in centimetres alongside the couch, with the zero corresponding to the level of the symphysis pubis. Fluids were usually introduced by the tap *h* (fig. 1) so that the manometer *f* attached to the pressure chamber recorded during introduction a pressure which was a resultant between the vesical pressure and the reservoir pressure. When the tap *h* was closed this manometer recorded vesical pressure alone. The other manometer, attached to the pressure chamber *l*, would continue to record true vesical pressure whatever the fluctuations taking place in *f*. In order to keep the pressure of input of fluid constant the reservoir was held by hand next the vertical scale so that its fluid level remained constantly opposite the required height. A mechanical arrangement for this purpose was found unsatisfactory owing to the unavoidable friction of pulleys.

Fluctuations of pressure were readily and accurately revealed by the manometer attached to the pressure chamber *f*, owing to the wide communication it maintained with the interior of the urethra. The ureteric catheter *b*, on account of its narrow internal diameter, offers some resistance to movement of fluid rapidly in either direction. A slight fluid impact at the tip of the catheters was found to be transmitted to the manometer attached to the small ureteric catheter with a latency of some 0·01 sec., and to the manometer attached to the rubber catheter rather more slowly, about 0·015 sec., owing to the greater resiliency of the rubber. The movement of fluid commenced to record after a slightly longer interval in each, so that for the commencement of change of pressure the narrow lumen of the small catheter offered no recognizable error at our speed of recording. With changes of pressure of over 100 cm. water in intervals of less than three or four seconds the manometer of the small catheter showed some lag in reaching final values, but as such changes were rarely our experience the error is negligible, and when it occurs in the records it is indicated. Lagging of pressure changes owing to obstruction of the openings of the catheters by folds of mucous membrane tended to occur when the volume of the bladder was very small. The flat curves thus produced are readily recognizable. The high tension of the rubber diaphragm of the manometers, the lightness of the mirrors, and the small amplitude of movement ensured that the vibration frequency was of very high order, and no allowance need be made for overfling or vibration from this cause.

In order to avoid the confusion of too many parallel deflections the

excursion of two of the manometer images, those of the abdominal and rectal recorders, were arranged to show a downward deflection for rise of pressure, the others to show an upward deflection.

Dubois [7] pointed out that vesical pressures taken from the level of the symphysis pubis as zero show difference from pressure at the actual centre of the bladder. The error is slight and is a positive value with an empty bladder and negative with the distended bladder. The

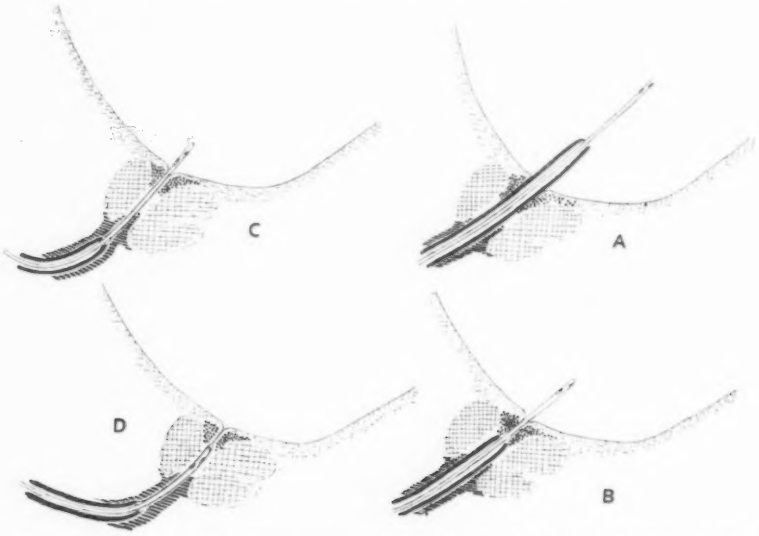


FIG. 2.—A diagrammatic representation of the means by which two catheters, one within the other, were used to measure the pressure within the bladder and different portions of the urethra. In A, both catheters are within the bladder and the large catheter prevents the activity of either sphincter. In B the larger catheter has been withdrawn until its manometer just ceases to record changes of vesical pressure produced by pressure upon the abdomen. In C, the larger catheter has been further withdrawn until micturition can be instantly controlled by will. In D, the catheters are further withdrawn until the pressure recorded by the smaller catheter is also no longer that of the bladder, but is still not directly influenced by willed effort.

values given here are uncorrected and thus should be comparable to those of Mosso and Pellacani, and most later workers. The symphysis pubis is much the most convenient base line for use in clinical work with abnormal bladders. In practice the catheters are passed, the bladder emptied by placing the reservoir at a negative pressure of − 20 cm. water, the pressure chambers of the glass adaptors are filled to a convenient level, and with the reservoir held with its fluid level corresponding to that of the symphysis pubis the manometer images are

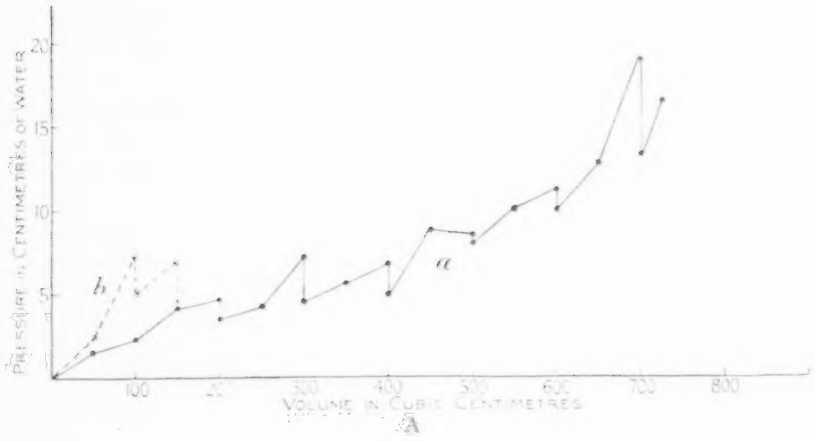
adjusted to fall on the base line of the moving bromide paper, before recording was commenced. The fluid used was sterile normal saline at reservoir temperatures of from 115° to 105° F.

Manipulation of the catheters secures variable disposition of their opening within the bladder and urethra, which are shown diagrammatically in fig. 2. The use of these dispositions is explained below. It was found that to maintain the dispositions shown in fig. 2 B, C, D, constant the catheters should be firmly held by the gloved hand of the assistant, otherwise they tended to move outwards during micturition.

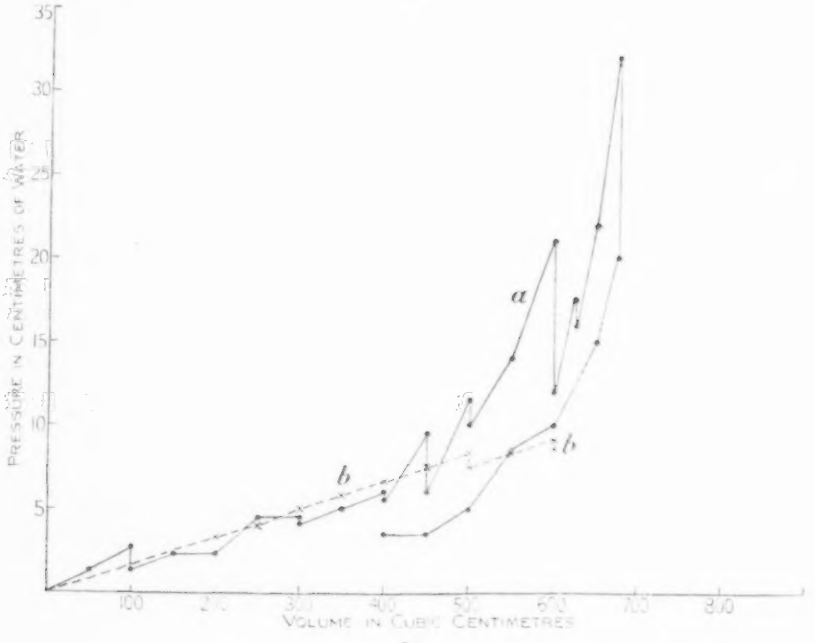
When the outlets of the system are closed, any contraction of the muscle of the wall of the bladder occurs under conditions of almost constant length of muscle fibre, a type of contraction called for convenience "isometric" contraction. With varying freedom of outflow the type of contraction has a variable isotonic property, though with this method no true isotonic contraction can be obtained. The advantage of the isometric record of any muscular contraction is the avoidance of distortion due to shortening, more cleanly cut relaxations, and more direct relationship between height of record and quantity of contraction.

(3) The Reaction to Distension.

The behaviour of the bladder during distension was similar in each of the three subjects. Our usual procedure was to allow fluid to enter the bladder through a narrowed aperture and under a constant pressure of 50 cm. water. The inflow was closed for an interval after the entry of each 100 c.c. in order that the vesical pressure could be observed under approximately isometric conditions. As each 100 c.c. of fluid was allowed to enter the vesical pressure rose gradually, to reach from 2·5 to 7·5 cm. water pressure at 100 c.c., and with gradual increments of volume reaching a pressure of approximately 10 cm. water at 500 to 600 c.c. (fig. 3 and Plates I, II). From that volume onwards the pressure rose more steeply to 18 to 20 cm. at 675 to 700 cm. (two subjects, Subject C not subjected to such high volumes). A slight fall of pressure during the intervals of rest at constant volumes under isometric conditions indicates the occurrence of a process of adaptation, a readjustment of vesical tension. This adaptation was definitely greater at higher volumes, and contrary to the conception of Mosso and Pellacani [18] was not in the nature of an adjustment to an almost constant tension of approximately 15 cm. of water but rather approaching a percentage adaptation of the tension induced by the previous filling. The graphs



A



B

FIG. 3.—Graphs of the relationship of the volume of the vesical contents to their pressure in the course of distension of the bladder. Fig. 3 A shows two curves obtained from subject A. The continuous line *a* is from data from the record shown in Plate I. The short curve *b* is from another experiment. The curves in fig. 1 B are from two experiments on subject B; the continuous line *a* is from the record of the filling shown in Plate II; *b* is from a later experiment, where the bladder had been very distended for some time before this filling. Each vertical fall of pressure indicates the degree of adaptation at a constant volume.

shown in fig. 3 reveal the variability of degree of relaxation of the tension exerted by the vesical wall following cessation of filling at different volumes. It will be seen from the graphs that resting vesical tension at moderate volumes varied from 5 to 10 cm. of water, and we have come to regard this range as the normal pressure of vesical contents. Acceleration of rate of filling increases the reactionary rise of tension, but, providing that attempted micturition does not occur, the pressure is still below 10 cm. at moderate volumes and the final adaptation reaches a pressure commensurate with the resting pressure for equal volume during slower filling. A *sudden* passive distension of the bladder often occasions a small reactionary wave (Plate III, fig. 3).

Adaptation of this degree necessarily implies the presence of a process of active vesical contraction before the adaptation occurs, for the bladder of the cadaver shows only a visco-elastic reaction (Osborne [20]). The argument is in fact exactly parallel to that by which the stretch reflex of voluntary muscle is demonstrated experimentally.

Distension of any viscus within the abdomen raises the intra-abdominal pressure. The muscles of the abdominal wall make an adaptation of their posture to changes of intra-abdominal pressure (Kelling [15]), and the effect of this adaptation is necessarily reflected and added to any adaptation made by the bladder. The extent of adaptation occurring in the experiments at present described may be gauged by the very slight changes reflected by intrarectal pressure (Plates I and II). The moderate speed and degree of adaptation therefore point to the existence of a mild tonic vesical contraction, induced by the process of distension, varying in degree with the rate of distension, and fading when distension ceases.

It will be noted that according to the shape of the curves the degree of this tonic contraction differs not only from subject to subject at comparable volumes, but also differs in the same subject at different times. For example, in fig. 3 B, *a*, the vesical tensions at volumes of from 400 to 675 c.c. were much higher during increasing volume than during emptying. Similarly in another experiment when the bladder had been distended for some time before the experiment by a volume of 827 c.c., a record of filling (fig. 3 B, *b*) shows volumes approaching those of the previous emptying shown in fig. 3 B, *a*. The curve in fig. 3 B, *b*, takes a rectilinear course which would appear to imply complete absence of any reaction, and must approximate to the curve of a completely paralysed bladder. This finding is in complete accord with Mosso and Pellacani's statement [18], that if the bladder has been very distended the tonic reaction at smaller volumes is for a time lessened.

There are certain exceptions to this mild reactive process. In Subject A, at or just below the volume of 100 c.c., and again at irregular periods (e.g., at volumes of 300, 450 c.c.), the resulting value of vesical tension showed regular fluctuations (Plate I). These waves of pressure appeared during filling; they were more frequent at the cessation of a filling, and gradually lessened in amplitude to complete disappearance. Rarely there was a single such fluctuation, as at a volume of 300 c.c. in Plate I. They were not accompanied by any sensation at moderate volumes, and appeared without the subject's knowledge. They were not directly related to the degree of vesical reaction provoked, as judged by the pressure immediately preceding or following the wave-like fluctuations.

The gradual rise in vesical tension as filling proceeds does not, at low volumes, intrude upon the consciousness of the subject. Introspection fails to bring any feature into conscious appreciation. We shall discuss later the sensations derived from distension at higher volumes.

In Subject A at a time when the vesical contents had reached 725 c.c. the pressure rose steeply in a wave to a crest pressure of 48 cm. (Plate I, *d*). This was accompanied by a sensation of increasing discomfort, so that the subject immediately exerted an effort to "hold water" by a voluntary contraction of the perineum and a strong-willed effort to postpone the sense of imminent micturition which formed a prominent feature of the accompanying compound sensation of discomfort. The rapid decline and disappearance of this wave disturbance was therefore possible evidence of its subjugation by an effort of will. That this had indeed taken place is further suggested by the recurrence of rising pressure soon after the subject had signalled that, the discomfort having in greater part vanished, the voluntary effort to overcome it was relaxed. There then occurred a disturbance reaching a high pressure (Plate I, *e*, *f*) which, though at first slightly modified by effort of will, proceeded to violent and painful vesical contraction which ceased only when a considerable volume of fluid had been expelled from the bladder.

In the Subject A there therefore resulted, as a consequence of continued distention of the bladder, a reaction which though at first modifiable by will had eventually the appearance and effect of an involuntary expression of vesical contents. The development of this process shows grades of transition from the mild wave disturbances observed during filling.

In one experiment on Subject B similar small fluctuations appeared

at times, usually as in Subject A, towards the termination of a period of filling (Plate II, after B, C, and *e*), but they were less clearly uncomplicated by movement of the abdominal wall. Although filling in this subject was carried on to a volume of 675 c.c. no vesical contraction reaching a high pressure occurred. Extreme discomfort experienced at this volume led us to abandon further filling. In Subject C the volume was not taken higher than 400 c.c. and no wave-like fluctuations of pressure were observed. We wished to spare this subject the possibility of discomfort and higher volumes were avoided.

(4) Modifications of Vesical Pressure induced by Willed Effort.

While the mild reaction of the bladder to filling at moderate volumes is accompanied by small waves of pressure without the knowledge, wish or consciousness of the subject, a willed effort to micturate may have a very definite effect. Subject B, when the bladder had been filled to a volume of 200 c.c. and with the system closed so that the volume remained constant, made a prolonged effort to micturate. This effort (Plate III, fig. 1) was in the nature of a relaxation of the perineum, with slightly increased tension of the abdominal wall. The immediate effect of this procedure was a slight fall in vesical pressure, presumably reflecting the fall in intra-abdominal pressure induced by relaxation of the perineum. After some thirty seconds the vesical pressure rose slowly and evenly to 30 cm. of water. The subject was then instructed to "hold hard" and to attempt to overcome micturition. The vesical pressure progressively declined to resting value, showing an acceleration after cessation of the effort to restrain. This acceleration of fall appears to be related directly to the relaxation of the perineum, and is interpreted as evidence that the tightening of the perineal diaphragm during the period of restraint had induced a small passive increase of intra-abdominal pressure which had corresponded with the falling vesical pressure.

The voluntary effort made by the subject in the attempt to micturate involves relaxation of the voluntary musculature of the perineum, and the subject himself is aware of the process primarily in a sensation derived from the perineal region. The manœuvre is introspectively that of letting go some faint holding of the perineum. The "holding" is not itself conscious except faintly by introspection, and the recorder of perineal movement reveals that the perineum continues to hold the same posture whether the subject be thinking of it or has his attention

directed elsewhere for long periods. The differentiation from a "strain" is important. If the subject be instructed to attempt to initiate micturition by "bearing down" the recorded events are altogether different. Such a strain in this subject produced only a progressive rise of vesical pressure in direct proportion to the amount of increase in abdominal pressure secondary to contraction of the abdominal wall and diaphragm (Plate II, F, G, H, and I). The perineum also contracted in some efforts (Plate II, *b*). A strain may be made mainly by diaphragmatic movement (Plate III, fig. 6, C). There is no independent change of vesical pressure.

The rise of vesical pressure in response to voluntary effort more commonly exhibits a fusion of waves. This type of facilitation is shown in Plate III, fig. 2, where no change in movement of the abdominal wall accompanies the development of vesical contraction. The vesical pressure is heightened in waves of increasing amplitude which fuse to form a plateau at 50 cm. pressure. A voluntary effort to overcome the disturbance resulted in a progressive fall of tension, commencing on this occasion four seconds after the abrupt movement of the perineal recorder indicated the onset of the perineal "holding" movement. A wave of pressure which commences just before the onset of the perineal contraction appears to run its course before relaxation commences. There is some slight undulation upon the decline of tension.

In Subject A the facilitation of appearance of waves of increased pressure was even more striking. In one experiment the amplitude and frequency of waves was directly proportional to the degree of voluntary effort to micturate. Thus, at a volume of only 100 c.c., when the subject was resting comfortably, but making a slight conscious effort to postpone a desire for micturition (which in this case followed a powerful contraction of the bladder induced a minute or two earlier) the vesical pressure remained very low, without spontaneous waves, and the perineum was contracted to a slight but definite degree. When the subject consciously relaxed the perineum and contracted the abdominal wall slightly, but determined that he should not encourage micturition (Plate III, fig. 4) the pressure rose slightly and a slight rhythmic fluctuation became evident. If the subject then thought of micturition and allowed sufficient relaxation of the perineum to cause a feeling that micturition was possible, but determined not to relax further, the pressure showed a series of regular waves reaching 20 cm. pressure at about twenty seconds interval (Plate III, fig. 5). These waves gradually lessened in amplitude and the condition reverted to the previous state.

If the subject encouraged such a desire for micturition by a full relaxation (still avoiding any active effort to express urine) a large wave of pressure develops with surprisingly short latency and requires sudden and intense voluntary conquest by "holding" to prevent its development into a painful spasm (Plate III, fig. 5, B, C, D). This facilita-

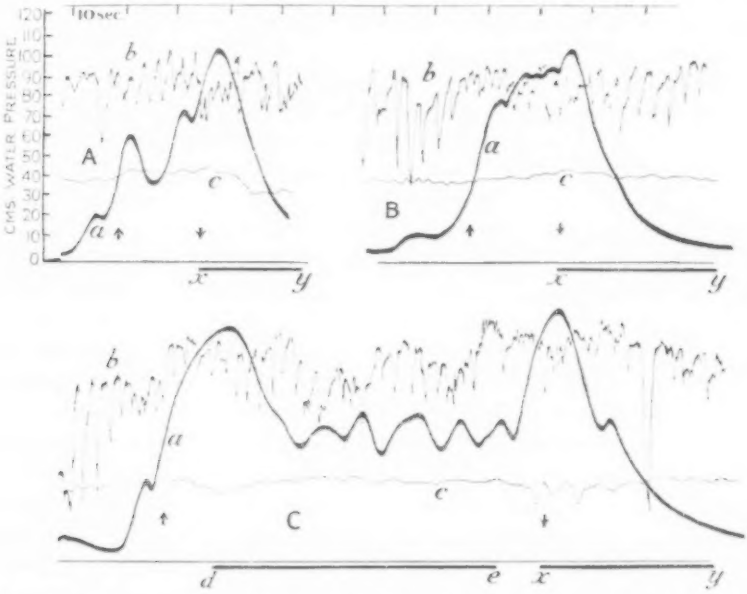


FIG. 4.—Three records of micturitions in response to voluntary effort, from a series obtained from Subject A during one experiment. The vesical pressure is shown by the heavy curve *a*, the movements of the abdominal wall by the irregular tracing *b*, and the changes of intra-rectal pressure by the curve *c*. The curves read from left to right. The vesical pressure is shown on the scale in cms. of water. The commencement of the rise of vesical pressure in each of the micturitions occurs in response to an effort commenced some seconds earlier. The occurrence of discharge from the sphincters (disposition as in fig. 2 C) is shown as a small arrow directed upwards. The abrupt cessation of discharge is indicated by an arrow directed downwards; it occurs in response to the onset of a powerful effort to restrain micturition made in the period *x*—*y*. In C, a less powerful effort to restrain, corresponding to the line *d*—*e*, does not secure complete closure of the sphincter, although it is accompanied by a rapid lessening of the vesical pressure and the appearance of rhythmic fluctuations.

tion of vesical contraction, under isometric (constant volume) conditions, by a willed effort, develops shorter latency and greater amplitude with repetition, so that the interval before its commencement after an accurate signal of the onset of voluntary effort may be extremely brief (1·6 sec. measured from the first indication of perineal movement in

Plate III, fig. 7 A). Some evidence of rhythmical waves in the course of a willed vesical response has been seen (Plate III, fig. 2). In a series of such responses all transitions are seen from simple waves, such as those in Plate III, fig. 6, to simple compounds (fig. 4 A in text, and Plate III, fig. 5 D, and 7 E), and varying degrees of fusion of plateaux (fig. 4 B). From smooth fused curves willed effort of restraint, when mild, has occasionally the surprising effect of throwing into relief a rhythmical substratum (fig. 4 C). Thus waves are dissected from more perfect compounds by the process of inhibition.

An isolated large vesical contraction induced by will is evidently a compound of small waves of moderate frequency (6 to 12 a minute). Mild facilitation will induce the appearance of such compounds in rhythmical series at a frequency of three to four a minute. It is not possible to determine from these experiments whether each wave in a compound is an expression of contraction of the same muscle fibres, but from the tensions developed it would seem necessary that this should be so. The muscle is thrown into virtually a tetanic contraction in which wave after wave fuses with its predecessor. We have seen such waves reach a tension of 260 cm. water. The smaller waves show marked resemblance to the single twitch of the bladder of the cat recorded by Stewart [27].

The conquest of large vesical contractions by an effort of will presents some features of unusual interest. In Subject A it was possible to record the effect of exertion of a maximal effort to overcome the contractions with different intervals of onset of that effort after commencement of the contraction wave. If the effort to overcome commences at the very onset of the wave of contraction the wave runs a regular sharp single peaked course, followed by a relaxation nearly as steep (Plate III, fig. 6 A). The commencement of the effort at any later moment up to just before the crest of the wave (Plate III, fig. 7 B) results in a wave of similar form and time relations. An effort exerted at the crest of the wave is too late to prevent the occurrence of a wave approximately double the size, presumably due to a second superadded wave which takes a course similar in time relations to the first wave, and already in course of development at the moment of onset of restraint (Plate III, fig. 6 E, 7 E, 6 *b* and 5 C). Large waves are often demonstrably compounds of smaller waves superimposed crest upon crest, though the ascent is at other times so steep that no fusion points can be detected. The effect of maximal voluntary effort to restrain is therefore eventual steep and complete relaxation if the effort is sustained, but it is apparent that once a single wave is in progress it cannot be cut short. The explanation

for this varying latency may rest upon some peculiarity in the process of development of inhibition in the mechanism of rhythmical excitation, but we prefer the simpler provisional explanation based on the supposition that each wave represents a volley of discharge of nerve impulses into the vesical musculature. Once such a volley of discharge occurs the slow muscular contraction is inevitable, and not influenced by inhibition. There would appear no necessity to relate this powerful inhibitory effect to the feeble and altogether doubtful potentialities of the hypogastric nerve.

It may here be pertinent to emphasize that from its nature as a hollow organ of which the motor effect is directed upon its contents, it is an *a priori* necessity that if any contraction occur it should occur in every part of the wall at one moment. This is in fact readily observed in the animal bladder to be the case, for the organ, unlike the bowel, does not move over its contents, it contracts as a whole or relaxes as a whole, except under the artificial condition of stimulation of a nerve belonging to one side of it. It is therefore a legitimate conclusion as a first step in analysis that each wave of pressure of the contents of the organ represents an active contraction distributed evenly throughout the wall. Further, since vesical muscle is composed of discrete, entirely separate fibres, such a response, accurately timed to occur in them all, must necessarily be the result of an outgoing nervous impulse adequately co-ordinated in time in the effector neurones concerned. In the bladder isolated from its connections with the central nervous system feeble spontaneous contractions of the muscle can still be obtained (Stewart [27]), but are not co-ordinated. Any regularity of rhythm resembles then the beating of but a few fibres. For the purpose of the analysis of the present records therefore it is possible to conclude that the effect of voluntary facilitation of contraction of the urinary bladder is to throw into activity the spontaneous synchronous "beating" of the motor neurones lying in the vesical plexuses and wall of the bladder. The thickness of the vesical wall allows fluctuation in intensity of contraction both by variation in the number of layers or fibres taking part in the contraction, and also by variation in frequency of nerve impulses being discharged into the muscle fibres.

It is not within the scope of our experimental method to determine the precise mechanism of that smooth tonic contraction which results from moderate distension and which by its partial relaxation determines adaptation. We see no objection to the supposition that it is the result of the excitation of small groups of muscle fibres throughout the organ

in such a way that some are always coming into contraction as others relax, a consequence of a continual "peppering" of impulses as has been conclusively demonstrated to occur in postural contraction of voluntary muscle. The effect of voluntary willed effort would appear therefore to be an enhancement of the wave form of co-ordination which occurs subconsciously and involuntarily, the acceleration of the rhythm of co-ordinated discharge and the facilitation of its spread to more and more of the muscular fibres. All these features are found in the graduations of spontaneous vesical contraction, from which therefore the willed contraction reveals no features of difference in form. Voluntary inhibition of the process gives evidence that with very brief latency all motor discharge to the bladder-wall is caused to cease, and after the preceding muscular contraction has run its course relaxation of vesical tension occurs.

(5) The Modification of the General Reaction to Filling by Voluntary Reaction.

Subject A, whose graph of filling pressures is shown in fig. 3 A, showed in his first experiment no large voluntary facilitations during filling and only a large involuntary response at the termination of filling. When, immediately following upon this, the bladder was refilled and the catheters now arranged as in fig. 2 *c*, so as to obtain records of sphincteric function, it was found that discharges could be obtained at such volumes and later at volumes as low as 50 c.c. The details of the response of the sphincters will be discussed below, and here it may be remarked that each response was accompanied by a large compound wave disturbance evoked by a process of relaxation (fig. 4). Abdominal contraction was practised many times without any evidence of its setting up any process of micturition (Plate III, fig. 6, and Plate IV, fig. 5) even when superimposed upon mild vesical contractions already in progress (Plate IV, fig. 7, at B). Subject C, a hospital patient, had, though very willing to help the investigation, no particular interest in the results obtained, and no particular power of introspection. He invariably responded to the order to try and pass urine by a strain upon the abdomen, as shown by the tightening of his abdominal wall, the rise of rectal pressure, slight bulging of the perineum and a linear rise of vesical pressure. This procedure was unsuccessful in setting up vesical contraction, and was equally unsuccessful in subjects A and B. Subjects A and B, having more direct interest in the investigation, had found by introspection of their own sensations from normal micturition that the

primary process was always some relaxation of the perineum, and an imitation of this under experimental conditions formed the basis of the voluntary facilitation described above.

When Subject A was submitted to a second experimental filling at a later date his previous experience of a capacity to set up micturition at small volumes led him to attempt the manœuvre at low volumes during filling of the bladder, and here the immediate grading of facilitation of waves described in the last section was readily obtained. Moreover, once having obtained such control, Subject A was able to reproduce the phenomenon at will. He had not been able during his first filling to set up such contractions. He felt certain during the second experiment that, as the vesical volume increased, an effort, faintly voluntary to the degree of being almost completely unconscious, was being made continually to hold in check any rising process of voiding. Thus, the absence of any spontaneous disturbance upon attempted micturition during his first filling was referable to a mild inhibition of micturition probably inducing a mild perineal tension. An inability to relax this inhibition sufficiently completely and thus initiate the contraction response was therefore partly a lack of experience of the absence of gravity and the unusual posture, possibly combined with the effect of the distension of the urethra by the catheter. Once the initial unpleasant sensations of passing of the catheter had subsided the subject had no sensation of its presence unless he thought about it for a few seconds, or unless the catheter were moved. The slightest disturbance of the catheter provoked an unpleasant sensation referred to the glans and urethral orifice. It is possible that the absence of fluid entering into the most proximal segment of the urethra had made initiation of contraction at first difficult, but our subsequent observations fail to confirm this view.

It is noteworthy, therefore, and in our opinion of great value in consideration of the shape of the curve of filling pressures of a bladder, that the low type of curve with little or no evidence of spontaneous waves may be solely the result of apprehension and unusual posture upon a normal vesical mechanism. This is undoubtedly the explanation of the reaction of Subject C, who, though suffering no defect whatever in micturition under ordinary circumstances, was quite unable to produce either bladder disturbance or sphincter discharge under the conditions of experiment. Subject B likewise, in his first two experiments, was unable to produce other than small facilitations, and unable to produce sphincter discharge, though able to facilitate contractions in an experiment at a later date.

We conceive that under natural circumstances the process of initiation of micturition resembles much more a series of events such as is seen in Plate I, accompanied by increasing desire for micturition, postponement of the final development of the vesical spasm at will, and not absolutely complete suppression of waves in the intervals.

(6) The Sensory Experience of Vesical Distension.

Although the sensation of vesical distension in mild degree comes within everyday general experience, and that of more severe distension comes at some time within the notice of most individuals, these sensations are unusually difficult to describe in detail. The disagreeable stinging sensation of catheterization was felt within the penis, more intense towards the meatus, and greatest at the meatus. The passage through the posterior urethra was felt as an exacerbation of this sharp sensation and entry of the catheter within the bladder felt as a lessening of the sharpness of the sensation, which nevertheless persisted for some seconds and then eased gradually.

As the bladder is gradually distended by successive inflows of each 100 c.c. of fluid no sensation whatever is experienced by the subject even with careful introspection, until just before the volume of 300 c.c. is reached (just before 250 c.c. in Subject B). At this time there was faintly discernible on introspection a feeling of the presence of some slight pressure deep in the mid-perineum, likened by Subject A to a very faint pressure from within, and by Subject B to a faint sensation of pressure with movement, "like rivulets running down the urethra." This sensation was not constant, it lasted some few seconds, then disappeared only to return at intervals of some seconds and disappear again. Subject A when experiencing the sensation on a second occasion and then with knowledge of the experience of B, felt that he also could discern movement of the faint pressure and agreed that the sensation was well expressed by the word "rivulets." It was not comparable to any sensation in normal experience. This sensation was not associated with any particular change in the vesical pressure, was not felt with slight waves of pressure occurring just after the volume of 200 c.c. and continued to occur as adaptation was occurring after the volume of 300 c.c. had been reached. As filling proceeded between the volumes of 300 and 400 c.c. at 50 cm. input pressure and narrowed inlet the duration of these periodic sensations increases and the interval lessens. As the sensation developed the factor of movement became more obvious

(" as if some urine were commencing to flow down the urethra "). The vesical pressure remains low, rising slightly as filling proceeds and in both Subjects A and B, just before the volume of 400 is reached, the sensation had become much more definite, but not in any way unpleasant, and could be easily displaced from mind. Subject A described it as the feeling that he could pass urine if he wished to make the attempt. He thought that it was the association of the periodic rivulet sensation with a mild warmth referred vaguely to the distal portion of the penis. It was quite definitely irregularly periodic. Subject B thought the sensation was more continuous, " like a desire to pass water," and decided that he thought the rivulet sensation remained periodic and had more definitely a running fluid quality, while the fresh sensation formed a continuous background not associated with it. He too was able to displace it from mind at will. Both subjects felt that the sensation was a faint desire to micturate which was readily displaced from mind.

In Subject B the next sensation as volume increased was a definite but very slight feeling of abdominal distension which appeared suddenly after a rest for some minutes at a volume of 400 c.c. (Plate III, fig. 8). There is no associated change in vesical pressure, which was 8·7 cm. water at the time. The slight continued sensation of potential micturition and abdominal fullness, with occasional rivulets (now less frequent) remained unaltered until the bladder was subjected to more rapid distension by allowing fluid to run in at 100 cm. pressure and full inlet opening (from 450 c.c. to 500 c.c., and again from 500 c.c. to 600 c.c.). The sensation of fullness increased progressively during these fillings and the " rivulet " sensation again became more definitely running, with some admixture of imminence of micturition (slight " urgency "); the desire for micturition had fully developed. This sensation gradually vanished during the pause at the volume of 500 c.c. (Plate II) and was renewed from the commencement of filling from 500 to 600 c.c. During the later period it occupied the sensorium to such a degree that the subject felt a definite continuous necessity to check the desire. When the volume of 600 c.c. was reached Subject B felt distended, with a slight feeling of flow into the urethra, although there was no evidence that this was occurring. The effort of holding in check the desire for micturition included a movement of extension of the knees. The pressure had risen from 10 cm. of water to 22 cm. of water in sixty seconds. There were no fluctuations of pressure at this time. This sensation remained constant and when the volume later reached 675 c.c. the subject felt a necessity

to exert the greatest effort to withhold micturition of which he was capable. Nevertheless when he made an effort to micturate no change occurred. The desire to micturate had gradually merged into a definite pain referred vaguely to the perineum. On emptying the bladder with reservoir level at −30 cm. pressure these sensations passed off in the reverse order of their appearance and abdominal distension had become only very slight at a volume of 450 c.c. The intermittent "rivulet" sensation again became prominent as volumes of 650, 600, 550 and 500 were reached, but no evidence of waves of pressure or of "follow-up" contraction of the bladder appeared.

In Subject A the development of sensation after the first appearance of rivulets followed a similar course. As filling proceeded definite spontaneous waves of pressure made their appearance and at the onset of one of these (reaching 16·2 cm. water), at a volume of about 465 c.c., a sharp increase in the rivulet and warm sensation occurred, not outlasting the wave, and not occurring with other earlier and later smaller waves (13·7 cm. water). With a vesical volume of 500 c.c. Subject A felt that micturition could readily be initiated and a slight abdominal discomfort commenced to be readily perceived. The sudden onset of desire to pass urine, with enhanced urethral flowing sensation, was signalled during a period in which the volume was kept constant at 500 c.c. There is no change whatever in the records of pressure at this time. The sensation was abolished by voluntary postponement, but recurred at intervals of about a minute, then ten seconds (more acutely) and then a strong effort to postpone the desire abolished it successfully until filling had been resumed and a volume of about 545 c.c. reached (slow filling at 50 cm. input pressure). The sensation recurred at decreasing intervals with a more definite feeling of distension of the abdomen as the volume of 600 c.c. was attained (Plate I). With further filling he felt the necessity for continued conscious effort to withhold micturition at a volume of 635 c.c. The onset of the first wave of reactionary contraction of the bladder was associated with a slightly painful and unpleasant sensation referred to the perineum with a slight burning quality. The ultimate development of an undulating violent contraction of the bladder in this subject was associated with a renewal of this sensation in an extremely intense form, and it was then associated with a tingling, prickling sensation felt all over the body. During subsequent emptying Subject A felt relief from all sensation at a volume of 520 c.c.

Subject C experienced no sensation during filling of the bladder until the volume of 175 c.c. was reached, when he complained of a discomfort

referred to the penis. With a volume of 200 c.c. he complained of similar discomfort, and again at a volume of 300 c.c. None of these sensations was associated with accompanying change in vesical pressure. On questioning he said he suffered no continued discomfort during filling up to 420 c.c., and subsequent emptying, though he had some sensation of slight distension at 420 c.c. The discomforts complained of were, in our opinion, probably all due to some movement of the patient with consequent movement of the catheter. They were all referred to the meatus. Subject C was an unsatisfactory witness as regards sensations and was evidently much concerned lest the sensations felt during catheterization recurred, and seemed unable to take account of milder sensations.

It is remarkable that a periodic sensation such as the "rivulet" response reported by Subjects A and B was not associated with any periodic change in vesical pressure. Though it was definitely enhanced at certain stages of filling and emptying of the bladder and might thus be thought to be derived from an appreciation of the passage of fluid through the catheter, it was definitely appreciated when no movement of fluid was occurring. We are not inclined to believe that it was derived from the periodic entry of fluid into the posterior urethra, for it occurs at such very low pressures at which, from our subsequent experiments on the sphincters, we are inclined to believe the sphincters both remain closed. Moreover, at these pressures a leak around the catheter of even one drop of fluid was never found to occur. The sensitive manometer should have been capable of detecting any rhythmic entry and regurgitation of fluid within the boundary of the internal sphincter. The "rivulet" sensation, the sensation of abdominal fullness, and the desire to micturate are none of them painful.

The desire to micturate can also appear periodically without accompanying variation in vesical pressure. The afferent stream of information from the bladder must under these circumstances remain constant. We see, therefore, no other alternative than that the abolition of the sensation of desire to pass urine and its subsequent return are processes taking place at a cortical level, and not associated directly with the process of fluctuation in vesical pressure unless that assumes a certain degree. We consider that the fluctuation of the "rivulet" sensation is likewise a cortical fluctuation in the appreciation and interpretation of an extremely mild visceral sensation. We have not experienced this "rivulet" sensation apart from experimental conditions, and therefore are unable to assign to it any definite place in normal vesical sensation.

In a later experiment Subject B remarked the extremely indefinite character of this sensation.

It has been described how, on some occasions, with an unusually sharp wave of vesical pressure the rivulet and running sensation were momentarily enhanced. In the second experiment with Subject A at a time when the outlets were closed, large waves of vesical pressure could be facilitated by will. These reached pressures of well over 100 cm. of water (Plate III, fig. 7). They were each associated during their onset with the rapid development of a sensation of distension deep in the abdomen, a "running" vaguely deep in the perineum and a sharply increasing discomfort referred to the whole perineum. With large contractions the discomfort was felt to be developing into imminent pain so that the subject felt urgently constrained to overcome the process. It is evident, therefore, that the development of a large enough active contraction of the bladder could reproduce the sensations derived from slow passive distension.

The sensation derived from restraint of micturition appears to be solely that due to high tension of the contraction which is suddenly converted from isotonic conditions to isometric.

From the description of vesical sensation served by the hypogastric nerves, from cases where these nerves alone remained in connection with the bladder (Riddoch [22]), it would appear that any or all the sensations described above may reach the spinal cord by these nerves.

(7) The Vesical Sphincters.

Although alteration of the disposition of the catheters to allow closure of one or both sphincters provoked some discomfort to the subject, this discomfort died away in the course of some three to five minutes. In spite of the uneven distension of the posterior urethra and of the presence of the fine ureteric catheter within the internal sphincter no discomfort of any kind was felt apart from some slight scalding as the first jet of fluid passed the sphincter during the first few micturitions. At first this slight scalding caused the subject to exert a momentary interruption in the early course of micturition (Plate V, fig. 9), but he could minimize it after one or two micturitions, and it finally disappeared. No discomfort was felt in the subsequent course of micturition.

With the catheters withdrawn to the disposition shown in fig. 2 C, and the outlet (*h*, fig. 1) of the urethral catheter opened slightly, the

record of a complete micturition is shown in Plate IV, figs. 1 and 2. With the signal to relax the perineum there occurs a slight bulging of the perineum and within a short interval the vesical pressure commences to rise, at first slowly and then more steeply, merging into the sharp ascent of a large wave. This rise is most often unaccompanied by any change in the posture of the abdominal wall, or in intrarectal pressure (see especially Plate IV, fig. 2). Early upon the rise of intravesical pressure the sphincter opens at first gradually and then swings steeply to maximal discharge.

Apart from the preliminary jerk of closure which tended to occur in the first micturition the subject made, and associated with a voluntary restraint, the sphincter opening was in general smooth and regular. The undulations which are found in the subsequent course of the urethral pressure reflect, with due allowance for distortion of the actual pressures by the outflow leak, the changes in pressure proceeding in the bladder. Thus after the initial very sharp opening the curve of outflow pressure runs parallel to the change of pressure within the bladder (Plate IV, figs. 1 and 2, and Plate V, fig. 9).

Throughout micturition the bladder remains in powerful contraction. As the termination of the response is approached there occurs a gradual diminution in the vesical pressure. The declining pressure is reflected in a similar decline in the discharge pressure which, however, terminates in an abrupt fall to complete closure. The vesical pressure shows often a further rise as the sphincter closes. This final rise in vesical pressure occurred only when the response secured powerful complete evacuation of a small volume of vesical contents (Plate IV, figs. 1, and 5 K). The remainder of the curve of vesical pressure is then rarely recorded in full, for the pressure usually either rises to extremely high values beyond the range of our recording paper as in Plate IV, fig. 1, or else the openings of the ureteric catheter were occluded by the close enfolding of the vesical wall, as in Plate IV, fig. 2. A more complete record of this "after-contraction" is seen in Plate IV, fig. 3, where a smooth sustained vesical contraction was followed to complete subsidence.

The only constant change which precedes the onset of the rise of vesical pressure with micturition is the relaxation of the perineum. There may be no change in movement of the abdominal wall and no rise in recto-colonic pressure. With the final "after-contraction" of the emptied bladder there is often a rise of intrarectal pressure, and, as in Plate IV, fig. 3, with the termination of a brisk and complete micturition, there is a tendency to suppress respiration and contract the

abdominal wall, but this is not either of necessary force or sufficiently constant in appearance to be held responsible for the "after-contraction" wave of vesical pressure.

The Commencement of Discharge.

The pressure at the moment the sphincter opens is not constant and is far below that at which it remains closed during a straining abdominal movement. In the series of consecutive sphincteric discharges observed on one occasion, Plate IV, figs. 4 and 5, the opening pressures were 23 cm., 25 cm., 18 cm., 30 cm., 40 cm., and 43 cm. of water. In such a series of successive responses each of which lessened the volume of the bladder, it is apparent that the vesical pressure at which opening occurs grows greater as the volume grows less. We have not found this inverse relationship between volume and opening pressure applicable in all circumstances, probably owing to the operation of other factors, such as facilitation by speed of filling and variation in the time interval between responses.

When an abdominal movement occurred during the facilitation of a discharge from the sphincter there was always accompanying evidence of perineal relaxation directly preceding concurrent active vesical contraction. On no occasion did the sphincter discharge in response to a passive increase in pressure, even if the catheters were arranged in the disposition shown in fig. 2 B, so that the internal sphincter must alone have been resisting, Plate IV, fig. 7.

In view of the reflex facilitation of micturition in the cat by the presence of fluid in the posterior urethra described by Barrington [4] it was of especial interest to determine the effect of the introduction of fluid into the posterior urethra when the catheters were disposed as in fig. 2 D. The bladder containing 70 c.c. of fluid, a volume at which the subject had previously readily provoked micturition, fluid was introduced into the urethra at a pressure of 100 cm. water. The distension brought no sensation to the subject and was quite ineffective in provoking micturition, even when he made a mild effort to micturate concurrently (Plate V, figs. 5 and 7).

Voluntary and Spontaneous Cessation of Discharge.

A sudden voluntary effort to withhold micturition during its course varies in effect according to the disposition of the catheters. Provided the urethral catheter were sufficiently far withdrawn, the discharge showed an immediate and complete cessation which we believe to be due

to the activity of the external sphincter. In this type of immediate voluntary cessation the curve of closure showed an initial small peak of increased pressure before the steep decline to zero (Plate IV, figs. 3 B and 8 E, G). This diphasic type of cessation is always of very brief latency after the signalled commencement of the voluntary effort, and occurs at the commencement of contraction of the perineal floor when that is recorded. If the discharge pressure be still rising when the effort of restraint is made the initial brief increase of pressure is less clear, but some trace of its presence is usually evident as in Plate IV, fig. 5 at G and H and Plate V, fig. 9 F. This type of closure once made can be maintained indefinitely by voluntary effort.

The restraint of vesical contraction when there is no fluid outlet is described in an earlier section. When discharge is occurring, with the onset of closure of the sphincter the vesical pressure often shows a rise to a sharp angle and then declines rapidly at first in a straight line and slowing later to reach resting value if the effort to restrain be continued (Plate IV, fig. 8, Plate V, fig. 9). This sharp angle superimposed upon the curve of vesical relaxation is clearly related to the change of conditions induced by closure of the sphincter, for the vesical wall closing upon diminishing contents abruptly meets the resistance of constant fluid volume. The lack of constancy in its occurrence is probably due to the smallness of outlet usually allowed, so that the bladder was not then diminishing in volume very rapidly. The remainder of decline of the vesical pressure follows the same curve as that following restraint under isometric conditions. The latency of closure of the sphincter is therefore much more brief than that of cessation of vesical contraction.

The preliminary positive wave in the diphasic cessation of discharge would appear to be due to a powerful contraction of the sphincter upon its contents and forceful extrusion of the contents before complete closure of the lumen occurs. The length of urethra embraced by the voluntary muscles of the external sphincter and the abrupt force exerted by its closure, thus endow activity of this sphincter with a characteristic type of termination of discharge. It does not seem to us possible that the M. accelerator urinæ could here participate owing to the presence of the catheter. The relationship of the position of the opening of the catheter to the external sphincter under these circumstances we picture to be that shown diagrammatically in fig. 2 C.

If the catheters be now introduced further, so as to bring the opening of the urethral catheter nearer the bladder, a disposition can be secured

where the response to a voluntary effort to restrain micturition becomes modified. The diphasic character of closure is lessened or completely abolished and only with very strong effort is the short latency of complete closure obtained (Plate V, fig. 1). At this level it will be seen that four efforts, each of which is accompanied by powerful contraction of the perineum, succeed in causing abrupt cessation of the outflow, without diphasic swing of the manometer. The fifth effort of restraint in the same micturition, though causing similar subsidence of the rising vesical pressure, secures only a few rapid fluctuations in the pressure of urethral discharge. The outflow continues and its gradual subsidence reflects only the declining vesical pressure which again rises as the effort of restraint is abandoned. The record of perineal movement reveals that the effort has been less powerful than the previous four efforts. There is therefore no sphincter closure. A sixth and slightly more powerful effort secures a complete and immediate closure of the sphincter. A seventh and last effort is less powerful and secures no immediate cessation, while after a delay the outflow shows a small brief interruption, followed by a deeper brief interruption, and after a similar interval a steep complete closure. With this disposition of catheters, therefore, the response to willed effort is modified in a manner which may be interpreted as interference with the full activity of the control of outflow by muscle under voluntary control. The activity of the mechanism which secures the delayed closure featured in the seventh effort of restraint in this record is elucidated by moving the catheters still nearer to the bladder, to a disposition which is shown diagrammatically in fig. 2 B. Here there is reason to believe that the opening of the urethral catheter lies between the internal and external sphincters. Records of the effort of strong voluntary restraint upon the course of micturition now reveal no immediate change in the pressure of discharge (Plate V, fig. 2). The vesical pressure commences to decline after some three to four seconds in response to the restraint, and with it the pressure of discharge. After one or two brief interruptions the discharge ceases abruptly, reaching complete closure in from seven to nine seconds from the onset of the effort, and at a time when the vesical pressure has shown progressive decline. This is further illustrated in Plate V, fig. 3, where, at a larger vesical volume and with more powerful vesical contractions, strong voluntary effort again has no immediate effect on discharge and after a long latency the outflow ceases abruptly. The delay in closure is greater and preliminary irregularity is less the more powerful the accompanying vesical contraction. This type of sphincteric closure

is therefore secondary to vesical relaxation. Further introduction of the catheter secures only a continuous record of vesical pressure, with no evidence of sphincteric activity (disposition in fig. 2 A).

It has therefore been found possible to secure a dissociation of the closing mechanism by arranging the catheters at two levels corresponding to control by the voluntary external sphincter on the one hand, and by the involuntary internal sphincter on the other. The existence of an internal sphincter in man has been doubted on anatomical grounds, for it is difficult to dissect a well-defined constricting ring such as is found in lower animals. The formation of a loop from the involuntary muscle of the detrusor covering the anterior wall of the urethral outlet as described by Heiss [14], appears to combine with a semicircle of involuntary muscle applied to the posterior wall of the orifice (sphincter trigonalis of Kalischer) (Wesson [28]), and thus a double loop of involuntary muscle participates in the sphincter. Whatever the actual mechanism of closure of the orifice our records leave us in no doubt that there is a proximal mechanism of constriction which is not immediately under voluntary control, and which serves a reciprocal relationship with vesical contraction. This sphincter is not forced by passive increase of vesical pressure (Plate IV, fig. 7).

The Combined Function of the Internal and External Sphincters.

The immediate closure of the voluntary sphincter in response to voluntary restraint as described above causes a complete cessation of outflow at a time when the internal sphincter must remain patent. Eventual closure of the internal sphincter under these circumstances can be at times registered. If the voluntary effort to restrain be sufficiently brief in duration, and micturition be allowed to proceed within some six seconds (Plate IV, fig. 8, at F and H, fig. 3, following A and B), recommencement of discharge is immediate, and the urethral pressure rises steeply again to a level representing intravesical pressure. Such a record appears to indicate immediate relaxation of the voluntary sphincter and resumption of full discharge, and it would appear unlikely that the internal sphincter had closed at all during the period of restraint. This is also seen after a slightly longer period in the second restraint in Plate V, fig. 4. It will be noted that under these circumstances the onset of the steep opening curve is preceded by a small downward dip, the explanation of which probably lies in the suddenness of relaxation of a tightly closed sphincter. The first restraint

in Plate V, fig. 4, shows the effect of a more prolonged effort. A small sharp jerk indicates relaxation of the external sphincter (C, D), and commencing resumption of outflow which ceases jerkily. The discharge recommences in a smooth curve of slow development (E) preceding the development of a fresh vesical contraction. The explanation of this type of reopening involves the assumption that the internal sphincter, secondary to the falling vesical pressure, has been about to close when the external sphincter relaxed. The final downward jerk at D is closure of the internal sphincter, and the smooth S-shaped reopening reflects the opening curve of this sphincter.

The effect of late relaxation of the external sphincter is shown again in Plate IV, fig. 5, where recovery from two long restraints shows a slowly developing urethral pressure on resumption of micturition, at E and H, revealing the gradual relaxation of the internal sphincter.

The internal sphincter therefore closes after a delay, not only when it alone controls the discharge from the bladder, but also when the external sphincter has already closed. The reciprocal relationship with vesical pressure is maintained.

With the catheters arranged in the disposition shown in fig. 2 D, it was found that, with a vesical volume of 70 c.c. and the subject not restraining, fluid introduced into the posterior urethra did not affect the pressure from the other catheter opening distal to the external sphincter, which therefore must remain closed under these conditions (Plate V, fig. 5), even when under these circumstances the subject relaxes the perineum in attempting to commence micturition, and even when an abdominal strain is added (Plate V, fig. 7). Under these circumstances fluid introduced into the posterior urethra under moderate pressure enters the bladder but does not pass out through the external sphincter which remains closed. The subsequent record of some vesical contraction in Plate V, fig. 7, reveals the eventual occurrence of vesical contraction in response to the continued effort to micturate with a filled bladder, but the urethral pressure does not rise until the vesical pressure is rising steadily and full micturition might be expected under any circumstances. With the same disposition of catheters in another experiment, the pressure chambers of both catheters being arranged to have a leak, the bladder having previously been filled, a micturition was allowed and the effects of the two sphincters recorded (Plate V, fig. 6). Here it will be seen that the internal sphincter opens earlier than the external sphincter, and in a more gradual manner (the narrow lumen of the ureteric catheter though not affecting latency in any recognizable

degree at this speed of record may nevertheless distort the actual curve of onset so that a sharp angle may be blunted). An effort of voluntary restraint closes the external sphincter in characteristic manner while the internal sphincter pressure declines slowly (Plate V, fig. 6 C). With cessation of voluntary restraint the external sphincter reopens at E, only to close again at F, as the internal sphincter is about to close gradually. The discharge is renewed and allowed to run its course to spontaneous cessation and again the external sphincter closes abruptly at I, leaving the internal sphincter still patent but about to close in a more gradual manner. An abdominal strain immediately after this (at K in the same figure) fails to disturb the pressure in the ureteric catheter and thus demonstrates that the internal sphincter has closed completely.

The external sphincter, therefore, not only closes first at natural termination of a micturition but also remains closed even when an effort is made to micturate and the perineum is relaxed. It is only when vesical contraction has commenced and has reached a degree sufficient to be accompanied by opening of the internal sphincter that relaxation of the tone of the external sphincter, sufficient to allow the passage of fluid, occurs.

(8) The Reactions of the Rectum in Relation to Vesical Function.

A full analysis of rectal behaviour has not been attempted, but some points of interest emerge in our records. The passage of a balloon into the rectum produced a contraction of the rectal sphincter which was easily overcome. As the balloon gained entrance into the anal canal a sharp discomfort referred to the anus, associated with a desire to expel the foreign body, was experienced. When the balloon was introduced 7 to 10 cm. and then allowed to remain still, these sensations, over a period varying from five to ten minutes, gradually subsided and the subject was aware of a sensation referred to the anus only upon introspection. The feeling of defæcation was renewed by further movement of the balloon and distension of the latter caused a sharp return of the discomfort. During the experiment the balloon tended to move inwards so that its tip was as much as 19 cm. from the anus.

The record of rectal pressure shows variations in abdominal pressure, including those caused by respiration, and changes in rectal pressure induced by contraction or relaxation of the bowel wall. During abdominal straining movements the rectal tracing mirrors the vesical record (Plate II, F, G, H, I, and Plate IV, fig. 6). Rapid filling of

the bladder induced a slight rise of intrarectal pressure when the volume of fluid in the bladder was high. In Subject A the rectal pressure rose 8 cm. of water during filling to 600 c.c. In Subject B at the end of a prolonged filling to 725 c.c. the rectal pressure rose 3 cm. During a spontaneous wave of contraction of the bladder there is no constant change in rectal pressure. In the absence of a change of intra-abdominal pressure the rectal pressure remains constant. Perineal movement alone has but little effect upon the rectal pressure, a determined perineal contraction when the bladder contained 130 c.c. produced an inconstant slight rise in rectal pressure, probably explained by a concurrent increase in abdominal pressure.

Subjects B and C displayed no other variations in rectal pressure. During the series of discharges of the sphincters obtained in Subject A slight rises of rectal pressure without corresponding abdominal movement occurred with each vesical contraction. Such rises are seen in Plate IV, fig. 8. In one response this increase became much more definite and eighty-five seconds later, when the vesical disturbance had completely subsided, a series of three isolated rectal contractions occurred at intervals of approximately thirty-five seconds with no other concommitant phenomenon. Straining movements set up no such contractions. A large rectal contraction which raised the intrarectal tension by 32 cm. of water occurred during a period of filling of the bladder. At the same time the subject recorded "a feeling of rectal contraction, a desire to evacuate the rectum." Two such contractions, each accompanied by the same sensation, are recorded in Plate V, fig. 8. Sphincteric responses obtained later were not associated with a change in rectal pressure, but at the termination of the vesical contraction a mild spontaneous increase in rectal pressure sometimes occurred (Plate V, fig. 9 H), and this is here well contrasted with the effect of an abdominal strain which precedes the sphincteric discharge.

In a subsequent experiment the distance from the tip of the rectal balloon to the anus was 11 cm. instead of 19 cm. as in the above experiment. On this occasion no rhythmical contractions of the rectum were observed, but when full uninhibited vesical discharges of small volumes were being recorded (Plate IV, figs. 1, 2 and 3) a rectal contraction occurred as the bladder was contracting strongly after it had expelled its contents. In the third response, at the termination of complete expulsion, the intravesical pressure mounted to a higher level, and coincidently a sharp rise in rectal pressure of 32 cm. of water occurred and rapidly subsided. It is of interest to note that a perineal

contraction occurs synchronously and mirrors the rectal record. It may be concluded that the rectum or distal pelvic colon shows spontaneous contractions which vesical activity tends to stimulate.

(9) Discussion.

An outstanding problem in the physiology of micturition, and the key to full understanding of nervous disturbances of that function, is the determination of the means by which the bladder and sphincters, which possess a definite measure of autonomy, are subjugated to the control of will. The most direct approach to the question appears to be an analysis of isometric records of contraction of the vesical musculature. The degree of willed control of such contractions is not only dependent upon the degree of distension of the bladder, but also upon the amount of excitability remaining from previous events. Rapid increase in volume facilitates the effect of willed effort to micturate. Preceding suppression of a vesical contraction appears for a short period to give especial ease in the voluntary production of other contractions. A certain volume of contents is necessary before any evidence of voluntary effect can be obtained. In one experiment in Subject A, no evidence of voluntary effect was obtained with volumes below 600 c.c., on one occasion below 125 c.c., and another occasion 50 c.c. We may make a provisional assumption that an unconscious, and presumably spinal, vesical mechanism requires the stimulation of distension before voluntary control becomes possible. The varying degree of distension necessary at different times in the same subject, lessening in each successive experiment, suggests that the variability of threshold is related more to the fluctuations of psychological factors than to variation in the spinal vesical reflexes.

Extraneous and apparently unrelated factors such as unusual posture or embarrassing circumstances can completely negative willed control. The failure of Subject C to provoke any vesical disturbance by effort of will was complete at the volumes used. In no experiment was ability to open the sphincters present when no vesical contraction could be evoked. Failure of voluntary control implied failure both of vesical control and sphincter control. Unwilled, but nevertheless estimable, factors of a psychological order appears therefore to affect the function of micturition as a whole.

Micturition, to a greater degree than any other voluntary function, has a functional as opposed to an anatomical conception in the cerebral cortex. All will is directed to the complete act. Indeed Genouville [10]

has maintained that willed micturition is not comparable to voluntary movement at all, for it entails thought of the completed process, just as willed effort to salivate requires an indirect process. The question is discussed at length by Adler [1]. It does not appear possible for voluntary effort to be directed to either the bladder or the sphincter alone. An introspective analysis of micturition reveals a concept of a series of sensations each of which is extremely vague in definition, with the exception of a contraction of the abdominal wall. This latter we have shown, in full agreement with Mosso and Pellacani [18], to be unnecessary for the induction of micturition. The next most definite and constant perceptual event in the voluntary initiation of micturition is a relaxation of the perineum. The constancy of its relationship to the onset of micturition is demonstrated by records. Micturition or vesical contraction never occurred without movement of the perineum. The latency between the onset of perineal relaxation and the onset of vesical contraction varies within wide limits. When the latency is long as in Plate III, fig. 1, and Plate II, at V, there does not appear any possibility that the actual active movement of relaxation has any direct, immediate effect. We have found no evidence that the entry of fluid into the posterior urethra plays any part in initiating micturition or in vesical contraction. The only factor of importance arising from perineal relaxation, therefore, would appear to be the continuance of a relaxed posture of the muscles. This movement of the voluntary muscles which surround the urethra appears to support Müller's [19] theory that there is reflected from them an afferent stimulus which exerts a reflex effect in evoking vesical contraction. The conception was furthered by the description of mild reflex stimulation of vesical contraction by distension of this portion of the urethra in animals by Barrington [4]. The effect of distension by fluid was in our experiments negative, but the possibility of a proprioceptive afferent stimulus for the reflex arising from the muscles themselves is difficult to exclude. We would stress, however, that perineal relaxation is not always effective in provoking vesical contraction and occurs in circumstances, such as straining at stool, when micturition is in abeyance. The movement of the perineum may be considered provisionally as an "associated movement"—resembling the movement of the ears when moving the eyes to one or other side, or movement of the arms in yawning.

The degree of voluntary control of vesical contraction, once psychological factors are negatived and the volume of contents brought to a moderate value, is most striking. The observed latencies in these

experiments may be very short indeed and give an impression of a degree of control much more complete for excitation of vesical contraction than was suggested by the work of Mosso and Pellacani [18]. Comparison of various degrees of vesical contractions produced by willed effort shows every stage from simple enhancement of involuntary rhythmic fluctuations, more or less complete fusion of such small waves, to smooth powerful high-tension contractions. Graded voluntary suppression of vesical activity reveals the reverse decomposition. It would seem, therefore, that voluntary control is expressed by the facilitation or inhibition of a local contractile mechanism related to co-ordinating neurones of the antero-lateral horns of the lumbosacral cord.

These "voluntary contractions" of the bladder present, therefore, two peculiarities by which they differ radically from all other voluntary movement. They require conditions which evoke spontaneous activity of the local mechanism, and even when these are fulfilled they can be completely in abeyance despite the most earnest effort of will. Furthermore, they reveal even in their most developed form the rhythmical character of the simple involuntary response of the organ. Though varying grades of intention to micturate could facilitate varying degrees of response, it was also found that the subject had only a vague notion of the degree of effect he was about to produce in any given attempt. Control of magnitude of response inevitably involved the employment of some admixture of restraint, and as far as introspection could determine was composed of a voluntary effort to micturate, itself but little variable, mingled with varying magnitude of restraint.

In marked contrast to the facilitation of vesical contraction lies the manner of its suppression. Apart from the ultimate reaction of the most extreme distension, a full-willed effort of restraint of micturition could, after a brief latency, secure complete abolition of vesical contraction. Voluntary suppression of vesical activity is absolute and unequivocal. The latency is such as may reasonably be supposed to represent the intrinsic slowness of smooth muscle in reaching the decline of its twitch contraction. Restraint of micturition can further be graduated in infinite degree. It therefore appears certain that voluntary innervation can inhibit neurones correlating the activity of the contractile units of the wall of the bladder. Goltz [11] first showed that destruction of the lumbosacral portion of the spinal cord in animals was followed by complete abolition of vesical function. There is some evidence, therefore, that the nervous mechanism related to co-ordinated spontaneous vesical contraction includes neurones within the spinal cord. The site of voluntary inhibtion

may therefore be related to the sacral segments, and the insignificant inhibitory effect on the bladder resulting from stimulation of the nerve supply suggests that such is the case. The absence of power of voluntary restraint in men with sacral lesions described by Head and Riddoch [13] reveals no willed inhibitory function in the hypogastric innervation. The spontaneous activity which occurs in such cases moreover appears more directly related to the vesical plexus.

The conditions attached to the performance of voluntary facilitation of vesical contraction open considerable doubt as to the existence of any direct voluntary excitation of vesical contraction. It is profitable to consider whether the whole control of vesical contraction by will may be by means of varying inhibition of the natural contractile reaction of the local vesical mechanism. Thus the powerful contractions with brief latency which we have described can be interpreted as sudden rebound of the local vesical autonomic contractile mechanism following the onset of removal of a damping, inhibitory influence from higher nervous centres. Effort to micturate is on this view an effort to disperse an inhibitory suppression of micturition, consciously or unconsciously applied. It may be argued that the period of inactivity would on this view require conscious effort of control and the act of commencement of micturition would more obviously necessitate a release from control. The type of vesical contraction produced immediately following upon rapid distension of the organ is undoubtedly of this order. The subject allows a release from a restraint of which he is definitely conscious. We would urge that in the induction of all voluntary micturition there exists no immediate necessity for the postulation of a direct excitatory pathway.

The development of voluntary control of micturition in the infant strongly suggests that inhibition of micturition is not only the main function exercised by will in this connection but may be the *only* function. That the mechanism should develop a capacity to function without intrusion upon consciousness, and to emerge into and be banished from consciousness at will, may be readily likened to the same property possessed by the function of walking or running.

Our records of filling of the bladder reveal rhythmical fluctuation of vesical pressure occurring from time to time as filling proceeds, and also at intervals with constant volume. These fluctuations in the vesical contractile mechanism intrude upon consciousness only when they reach a certain degree of magnitude. Their suppression at higher volumes becomes a conscious act, but at lower volumes and when not provoked

by distension they disappear without any intrusion upon consciousness or variation in local conditions. If they are evidence of stimulation of the local contractile mechanism alone they should continue to occur in continuous series of increasing tempo. Their occurrence may therefore be regarded as variations in degree of involuntary suppression and further evidence of readjustment at an unconscious level.

These observations upon the modification of the automatic, probably reflex, activity of the bladder by willed efforts, have in our view a profound influence upon the interpretation of the volume-pressure curve as measured by the Rose cystometer, and used to estimate disturbances of vesical innervation [23]. The low flat curve pictured in fig. 3 B, *b*, is the curve of the distension of an organ so well subjected to higher nervous depression, that its behaviour appears identical with that of a paralysed bladder. Variation in degree of voluntary control can produce a higher curve, rising to irregular peaks if free contractions are allowed. The discomfort of powerful contraction appears to be of considerable importance in determining the flatness of the normal filling curve, and the interpretation of irregular variations of this curve requires consideration of the possibility of facilitations and restraints exercised by the subject.

When the analysis of micturition is further extended to include the function of the sphincters it becomes at once apparent that the one very definite factor of voluntary control of vesical activity, namely inhibition, has a direct counterpart in the sphincteric mechanism. Voluntary restraint of micturition occasions both inevitable cessation of vesical activity and immediate powerful, direct closure of a distal part of the sphincter. The obvious voluntary control of this sphincteric mechanism identifies it with the M. compressor urethrae, or external sphincter of Henle. Its activity in response to voluntary effort is documented in our records by a diphasic excursion of very brief latency, with an associated contraction of other voluntary muscles of the perineum.

The activity of the external sphincter in the course of voluntary initiation of micturition and its spontaneous cessation is of a different kind. Despite relaxation of other voluntary muscles of the perineum in the course of the effort to micturate, the sphincter does not appear to relax until after the internal sphincter has relaxed sufficiently to allow fluid to enter the posterior urethra. Distension of the posterior urethra by fluid does not secure relaxation of the external sphincter even when combined with voluntary effort to micturate. The external sphincter appears, therefore, to maintain a tonic contraction subject only to

relaxation of the internal sphincter or contraction of the bladder. Young [29] maintains that the external sphincter remains closed if the internal sphincter is dilated by an instrument especially adapted to the purpose. Direct relaxation of the internal sphincter therefore appears to be the only factor determining relaxation of the external sphincter.

Our experiments have confirmed the work of Rehfisch [21] which revealed the continuous function of a closing mechanism proximal to that which is subject to direct voluntary control, and we would identify this with the internal sphincter of Henle at the neck of the bladder. We have found that this sphincter not only opens on effort to micturate, but also can close following effort of restraint. Such closing and opening may continue until the bladder is emptied.

The internal sphincter cannot be induced to open without the presence of vesical contraction, and we consider this finding to be one of considerable importance to the full understanding of the process of micturition. Passive increase of intravesical pressure does not alone suffice to render the sphincter patent, however great the volume embraced by the bladder. Not only is the relaxation of this sphincter related constantly to the accrescence of vesical pressure, but its closure is a process inseparable from the occurrence of vesical relaxation. The function of the sphincter is reciprocal with that of the vesical wall. The opening of the sphincter occurs earlier on the rising wave of vesical contraction, and its spontaneous closure earlier upon the decline of the wave, the greater the volume of fluid in the bladder, but no other effect of variation in volume was observed. Closure of the internal sphincter is directly related to subsidence of vesical contraction, and the characteristic delay in the response of this sphincter to willed restraint is the outcome of this relationship.

Voluntary inhibition of vesical contraction brings about an indirect closure of the internal sphincter. There is some evidence that the sphincter contracts in a series of rhythmical jerks as if it possessed an inherent contractile rhythm several times more rapid than that of the smooth muscle of the bladder. There is no evidence that it reacts in a manner other than the direct inverse of that of the detrusor muscle of the vesical wall. Though there may be minor lessening of contraction of the sphincter accompanying minor contraction waves in the bladder (Schwarz [24]), our method allows only the registration of the moment the lumen becomes patent so that it is not unlikely that the sphincter contraction may reflect the direct opposite of the vesical contraction without any especial arrangement to adjust the occasion of its opening.

The work of Wesson [28] and the illuminating suggestion of Young and Macht [30], that a slip of the muscle of the trigone actively dilates the internal sphincter, provides a means whereby contraction of the vesical trigone actively tends to open the internal sphincter. Our method of experiment does not allow a direct opinion upon the question, but the evidence from physiological experiment upon the internal sphincter of animals such as the cat provides ample evidence of the existence of a direct reciprocal innervation of detrusor and internal sphincter. The reciprocation between the bladder and external sphincter has probably a reflex basis, the fifth reflex of Barrington [4].

The final event in micturition, if the bladder reach complete evacuation, consists of a complex abdominal, vesical and rectal contraction, associated with slow closure of the internal sphincter and a sudden closure of the external sphincter. The external sphincter appears to close first.

Normal sensation from the bladder is derived in part from the tension to which the vesical contents is subjected. Mosso and Pellacani [18] and Genouville [10] would relate all sensation directly to the intensity of vesical pressure, while Guyon [12] showed the fluctuation of sensation with waves of contraction of the bladder. When the volume is progressively increased there is evoked a series of sensations with the vague reference which characterizes all visceral feeling, and culminating in actual pain. These sensations are not in our experiments directly related to the pressure of the vesical contents, for powerful passive pressure upon the bladder when the volume is low gives rise to no such sensations as occur when the volume is increased, though the pressure may then still remain quite low. We have not found a pressure of 18 cm. of water necessary to evoke desire for micturition, indeed discomfort may be extreme at much lower pressures. Sensation is not necessarily evoked by a spontaneous vesical contraction, though if the volume is such as to evoke some sensation such a contraction determines an immediate increase of it. If the active vesical contraction be sufficiently powerful the whole series of sensations to acutepain may be experienced as the contraction gains tension, though the volume remain so small that the resting bladder gives no sensation at all. The sensory end-organs concerned therefore have an adequate stimulus both in passive increase in length of muscle fibre and active increase in tension, and by some means these can sum their stimulation in infinite series. The resultant sensation, if moderately constant, can by some process be suppressed from consciousness. We have found no

evidence to support the contention first brought forward by Goltz [11] that desire for micturition is produced by the entry of fluid into the posterior urethra. Fluctuations in its perception do not necessarily reflect equivalent fluctuations in either degree of distension or active contraction, and this type of variation in sensation presumably possesses a psychological basis.

The process of storage of urine and its evacuation occurs, therefore, in a reservoir of which the distension excites a tendency to an automatic discharge. The primary factor in discharge is contraction of the wall of the bladder with an accompanying secondary reciprocal relaxation of both sphincters. The control of discharge and the utilization of the reservoir for volumes above about 50 c.c. depend upon unconscious and conscious inhibition of vesical contraction. If necessary this may be reinforced by active voluntary excitation of the external sphincter until the vesical contraction is overcome. More usually the process pursues a course of progressive complete adaptation without the occurrence of sufficiently powerful vesical contractions to be accompanied by full relaxation of the internal sphincter until conscious and unconscious control of vesical contraction is released by a voluntary effort.

(10) Summary of Conclusions.

(1) A method is described by which records of the pressure within the normal urinary bladder may be obtained during manipulations of the volume of the organ and during micturition. By this method it is shown that the human bladder reacts to distension by contraction of its wall.

(2) The reactionary contraction which is evoked by distension of the bladder is controlled by a restraining effect which at low volumes is subconscious in operation. This process of adaptation, or modification of reaction, intrudes upon consciousness in greater degree as volume increases.

(3) The normal sensations perceived are set up by the process of adaptation only when the active vesical contractions concerned reach a threshold intensity. Otherwise sensation is derived from passive enlargement of the organ. Sensation is thus only indirectly related to pressure, and in such a way that increase in area of vesical wall (increase of length of muscle fibre), within limits of only very slight corresponding increase of passive internal pressure, markedly lower the threshold at which added spontaneous active contractions can produce sensation.

(4) Apart from a faint background of maintained tonic activity,

spontaneous vesical activity takes the form of waves of contraction appearing in rhythmical progressions.

(5) Willed effort to micturate can evoke powerful contractions of the bladder with very brief latency of development. These contractions in their form and rhythm differ in no way from the spontaneous reaction of the viscus.

(6) Relaxation of the musculature of the perineum appears to be inseparably associated with the voluntary development of micturition. It is not regarded as an essential factor of the process but as a closely linked "associated movement." It is not accompanied by relaxation of the external (voluntary) sphincter. Contraction of the abdominal wall is a less closely associated movement which can be dissociated from micturition completely. A tendency to spontaneous activity of the rectum and lower pelvic colon is a much less common association with micturition.

(7) Voluntary restraint of micturition has a direct effect on the contraction of the bladder, so that the spontaneous nervous discharges responsible for vesical contractions can be completely inhibited with ease. It is suggested that the site of impact of this inhibition is on outgoing neurones of the spinal cord. Contraction of the perineal musculature is closely associated with voluntary restraint as is also direct and immediate closure of the external sphincter.

(8) The internal (involuntary) sphincter contracts and relaxes in reciprocal relationship with the detrusor muscle of the wall of the bladder. It is not under voluntary control, and its reaction to voluntary effort to control micturition is entirely secondary to the effect on detrusor activity. The closure of this sphincter is definite, and is continuously maintained during intervals of slight or absent vesical contraction.

(9) The external (voluntary) sphincter is also maintained in closed posture and opens only after opening of the internal sphincter. It closes spontaneously at the termination of micturition before the internal sphincter has closed. Closure in response to effort of will is more powerful. It appears not to be relaxed by voluntary effort.

(10) Normal micturition is entirely secondary to active contraction of the bladder. From the direct nature of the effort of voluntary restraint and the indirect nature of voluntary facilitation, voluntary control of micturition is regarded as being effected solely by variation in voluntary and subconscious inhibition of the mechanism of spontaneous reaction to distension.

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PARENCHYMATOUS CORTICAL CEREBELLAR ATROPHY (CHRONIC ATROPHY OF PURKINJE'S CELLS).[1]

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Introduction.

It is by no means easy to obtain a clear understanding of all that is included under the term cerebellar atrophy. In the literature available on the subject are many poorly organized reports dealing both with the clinical aspect and the pathological findings after death. Assumptions based on deficient anatomical inquiry go hand in hand with the most meticulous pathological research of material lacking all or almost all clinical features. Classifications based on a mixture of clinical and pathological factors and without criteria to guide their destiny appear in every article on the subject, and to a student commencing his labours they end in producing a state of confusion. Each writer on the subject of cerebellar atrophy has added his quota, and from the maze of types a few classifications remain that are helpful. Reference might be made to classifications by Mingazzini, Holmes, Archambault and the more recent one of Marie, Foix and Alajouanine. Each system of classification has been based on the sum total of knowledge acquired at the time it was made, plus certain ideas of the writers. To attempt a more modern classification, however, considering how far short knowledge of the subject of cerebellar atrophy falls, would result simply in further confusion. A few types of cerebellar atrophy remain nevertheless, and serve as outstanding examples, for the simple reason that in each instance the work of their delineators, including both clinical and pathological features, is reasonably adequate and satisfying. The progressive familiar type of cerebellar degeneration described by Holmes, the olivo-ponto-cerebellar atrophy of Dejerine and Thomas, and a type

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of cerebellar atrophy recently described by Marie, Foix and Alajouanine, serve as shining examples. The last-named type is the basis of the present consideration; it has been described by various observers in the past, and by virtue of its simplicity and clarity is entitled to fair consideration. Throughout the years since the first description by Murri in 1900 the type has been known by many names. Murri called it cerebellar degeneration due to intestinal intoxication, and recent writers on the subject, Kirschbaum and Eichholz, in 1932, described it under the caption of cerebellar cortical atrophy. Throughout this period of thirty-two years, fifteen cases have been described. Perhaps the most lengthy account of the disease was given by Marie, Foix and Alajouanine in 1922 with the somewhat lengthy name of primitive parenchymatous atrophy of the cerebellum of cortical localization. No matter how the names have varied from writer to writer, the clinical and pathological syndromes seem to have been essentially the same. Recently a case of this type of cerebellar atrophy has come under our observation and since relatively few cases have been reported in literature, and these mostly in foreign literature, we have deemed it advisable to review the subject again, and to record our experience, and our rather guarded views with regard to the ætiology. For purpose of clarity, the title of our contribution has been adapted from the English nomenclature and the name of the disease (parenchymatous cortical cerebellar atrophy) approximates closely that used by the American writer, Archambault.

Fifteen cases have been recorded by various observers. The widespread distribution of patients shows that no local factor can be responsible. Thus, one patient lived in Italy, ten patients lived in France, three in Germany and one patient in the United States. Since anatomical confirmation was lacking in two cases described by Rossi and in one case described by Marie, Foix and Alajouanine, these are excluded from consideration, especially since various diseases in the cerebellum may give a similar clinical picture. Another case described by Marie, Foix and Alajouanine is excluded for the reason that clinical data were lacking, and the case represented merely a pathological specimen of unknown origin. In one of Rossi's cases the findings at the necropsy were not mentioned, but it was included because later Marie, Foix and Alajouanine described the same patient who had since come to necropsy. Thus eleven cases remain that are representative of the essential characteristics of a disease, intriguing because of the simple clinical syndrome noted during life, and the clear-cut conditions in the cerebellum noted after death.

Clinical Characteristics.

In the cases recorded there did not appear to be any familial tendency, thus contrasting with the group of cases described by Holmes. Further, no other disease seemed to occur in the family that might have a bearing on the problem except in the case of Kirschbaum and Eichholz in which the families in the three preceding generations had been heavy drinkers of alcohol. The sex of the patient was recorded in nine of the eleven cases reviewed. Seven patients were males and two were females. The age of onset of the disease was after middle life in most cases. Nine patients were aged between 40 and 80 years, and the average age was 62, somewhat more advanced than the average of 57 given by Marie, Foix and Alajouanine. Two cases in the series, however, were different in respect to age at onset of disease. The patient described by Archambault had a severe illness characterized by gastro-intestinal disturbances and fever at the age of 17. Thereafter his upper and lower extremities were awkward and clumsy. Nevertheless, he was able to work and these difficulties did not increase until he reached the age of 40, when a slow and steady progression of ataxia occurred. In the case described by Kirschbaum and Eichholz progressive cerebellar ataxia developed slowly and insidiously; commencing at the age of 20 and progressing to the patient's death at 59. However, this condition was not very not noticeable until the age of 35. He was first in hospital at the age of 41 when he sought relief for his condition. He continued his employment as clerk until the age of 46 when he was pensioned, mainly because his handwriting became illegible. These two cases, therefore, differ markedly from the others in the age of onset and the life history of the disease. In most cases the disease appeared for the first time between the fifth and seventh decades and, therefore, after the prime of life, and when regressive changes are beginning to be manifest.

The mode of onset is usually gradual and insidious, the disease involving the body symmetrically, progressing steadily and slowly over a period of years to helplessness and death from intercurrent disease. The two cases of Murri and of Rossi are exceptions to this course. In Murri's case the disease was primarily acute with gastro-intestinal symptoms, and it ran a relatively rapid course to a fatal termination within nine months. In Rossi's case the condition came on acutely following diarrhœa; it improved after three months, only to relapse again into a more slowly progressive form over a period of eight years. Stender and

Lüthy's patient had had a stormy initial episode characterized by acute polyneuritis of alcoholic origin. This cleared in five months, leaving residual ataxia, which was stationary for fifteen years, but later progressed to a fatal ending. Excluding Murri's case, in which the course was unusually rapid, the average length of illness among the ten other patients was $13\frac{2}{10}$ years, constituting a chronic, long-drawn-out course.

The chief complaint of all the patients, as might be expected, was difficulty in walking. From descriptions of complaints and the clinical picture it would seem that the ataxia was of a relatively pure type, and that associated with cerebellar disease. The lower extremities were always much more seriously involved than the upper, at least in the earlier stages of the disease before the patient became completely helpless and bedridden. The gait was swaying and hesitating, with oscillations antero-posteriorly, compared by many observers to the staggering, reeling progression of an intoxicated man. The legs were spread wide apart to give firmer support, and often the trunk did not follow the progress of the legs so that the patient tended to pitch forward or backward. The hands were held to grasp at support, and many patients were forced to use canes, crutches or the support of a friendly arm. Some patients who fell could not arise without help, but once balanced they could stand alone. Various tests of the lower extremities with the patient lying or sitting showed dysmetria and dyssynergia, commensurate with the stage of the disease. An element of spasticity in the lower extremities was described by Kirschbaum and Eichholz, Jelgersma and Rossi, but this was never marked and was dominated largely by the cerebellar features.

In six of the eleven cases recorded the upper extremities were relatively unaffected in the disturbance of function so marked in the lower extremities. Marie, Foix and Alajouanine made a point of this and drew some interesting conclusions concerning cerebellar function by noting the corresponding site and distribution of the more severe lesions in the cerebellum itself. However, in five cases severe inco-ordination of the upper extremities was noted, and they were as functionally impaired as the lower extremities. The more severe examples of this involvement of the upper extremities are represented by the cases of Kirschbaum and Eichholz, Archambault and Jelgersma. Jelgersma stated that his patient spilled water when he raised a glass of it to his lips, could not untie a knot once he had tied it, and his handwriting, a specimen of which was shown, was almost illegible.

Although it is hard to separate clinically a so-called tremor from the

oscillations produced by cerebellar disease, apparently none of the patients had anything like a violent shaking of the limbs as might be seen in a disease such as multiple sclerosis. Jelgersma and Archambault described tremor of the head, again apparently part of the syndrome of cerebellar disturbance. The speech was affected in seven cases, and was variously described as being monotonous, drawling, slow, staccato and explosive; generally it was indistinct. In two cases it was apparently unchanged, and in two cases this function was not mentioned. Nystagmus was not marked in any of the cases; at the most there were a few unsustained jerks of the eyes on lateral deviation. In all cases the disease was symmetrical and equal on both sides of the body. An outstanding feature was the preservation of intelligence in all the cases reviewed and this persisted to the end. The actual cause of death of these patients was sought, since it is obvious the disease itself should not be lethal. In four cases the terminal state was not mentioned. Pneumonia occurred in two cases; chronic bronchitis, cardiac failure, carcinoma of the pancreas, cirrhosis of the liver and apoplexy were given as causes of death in the remainder of the cases.

Pathological Data.

In most cases gross atrophy of the cerebellum was reported. Archambault described the cerebellum as being reduced by a third, and Rossi found it reduced by a fourth and a fifth in two cases respectively. In two cases of Marie, Foix and Alajouanine it was diminished by a quarter. Stender and Lüthy, Lhermitte, Kirschbaum and Eichholz, and Thomas also mentioned that the cerebellum was smaller than normal, but the amount of reduction was not estimated. Nevertheless, in one case of Marie, Foix and Alajouanine and in Jelgersma's case, the volume of the cerebellum was described as being normal. Therefore, there seems to be no uniformity in this respect, and it is manifestly difficult to estimate by ordinary methods gross alteration in size of the human cerebellum.

In cases in which there was obvious atrophy, closer examination, particularly in the cases of Marie, Foix and Alajouanine disclosed widening of the sulci and both shrinkage and hardening of the individual foliæ. This also seemed to have a particular distribution according to intensity. It was more marked in the vermis and particularly in the supero-anterior portion. These changes diminished laterally and posteriorly so that the parts least affected in the cerebellum were the posterior and inferior portions of the vermis and the more lateral

portions of the lateral lobes. Thus, although the entire cerebellum may be affected, the superior vermis and quadrilateral lobule receive the brunt of the disease.

Microscopical examination showed first, under low-power magnification, that the atrophy was confined to the cortex, and except for minor changes in the white matter of the individual foliæ, the central white matter of the cerebellum as well as the dentate and other roof nuclei were normal. Under higher power the outstanding lesions of the disease were revealed, namely, a relative or absolute disappearance of the Purkinje cells, according to the area examined, with preservation of the basket structures around them. On this fundamental point all authors are agreed, and it may be seen that the disappearance of so large and conspicuous a structure as the layer of Purkinje's cells gives a characteristic appearance to the sections of the cerebellar cortex. The distribution of this destruction of Purkinje cells corresponded to the gross changes mentioned, that is, more intense in the region of the superior vermis and quadrilateral lobule. In these areas the Purkinje cells were absent. In other areas changes occurred signifying varying degrees of destruction with swelling, karyorrhexis, diminution in the intensity of the stain, eccentricity of the nucleus, and shrinkage, and finally only shadows of the cells remained prior to their complete disappearance.

The cortex, under moderate magnification, appeared to be thinned. The breadths of the granular and molecular layers were diminished, they stained less intensely and there was slight proliferation of neuroglia. The white matter of the folia appeared to be slightly rarefied, and according to Marie, Foix and Alajouanine it was sclerosed and this sclerosis ended with a line of demarcation where the white matter of the folia met the central white matter of the cerebellum. The latter structure was normal microscopically. More minute study by Bielschowsky's method and other silver stains showed the entire wiping out of the Purkinje cells with their plumes. The basket cells, climbing fibres, mossy fibres and T-shaped fibres were everywhere preserved. As a contrast, the plexus of fibres above and below the Purkinje cells, considered by Cajal as being retrograde collateral fibres, were, in conformity with this idea, absent. Marie, Foix and Alajouanine described atrophy and sclerosis of the postero-medial portion of the inferior olivary nucleus and mild degeneration of the olivary fibres. Stender and Lüthy also noted these changes. All other parts of the central nervous system were normal. With the exception of Archambault, all authors reported

PLATE VI.

FIG 1.

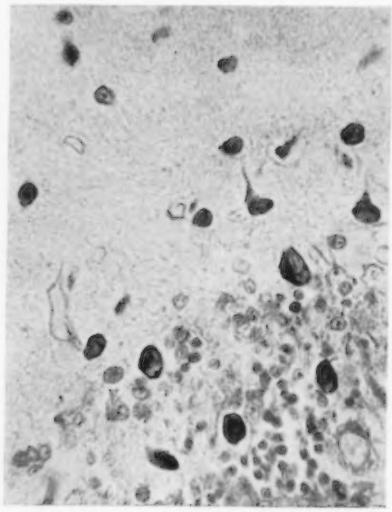

FIG. 2.

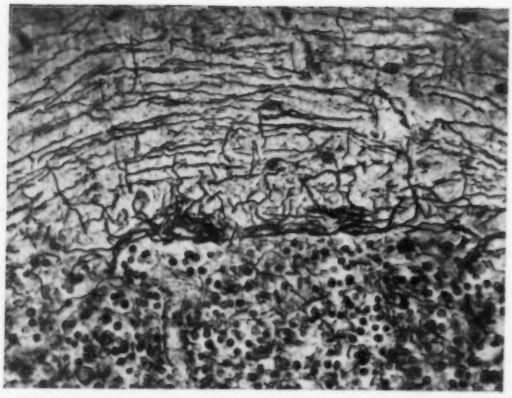

FIG. 3.

FIG. 1.—Gross atrophy was not present. The molecular and granular layers are intact, and there is no atrophy of the white matter. Meningitis was not present and the blood-vessels were normal (hematoxylin and eosin, × 8).

FIG. 2.—Several immature ganglion cells may be noted in close proximity to the Purkinje cell layer. The cells do not have dendrites or axis cylinders, but they have the characteristic nuclei and nucleoli as well as Nissl granules. Normal Purkinje cells are absent (thionin, × 550).

FIG. 3.—Absence of Purkinje's cells may be observed, but the baskets are well preserved. Tangential fibres in the molecular layer and also fibres in the granular layer may be noted (modified Orlandi silver impregnation method, × 300).

To illustrate Paper by Parker and Kernohan.

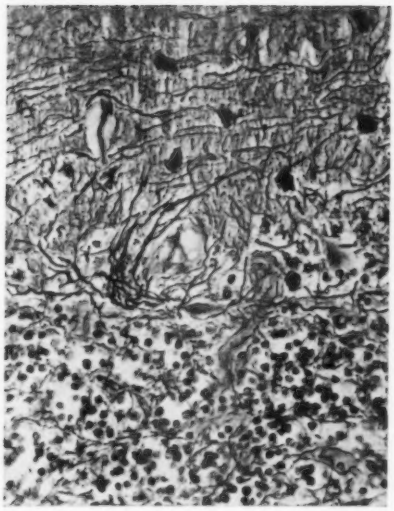

FIG. 4.

FIG. 5.

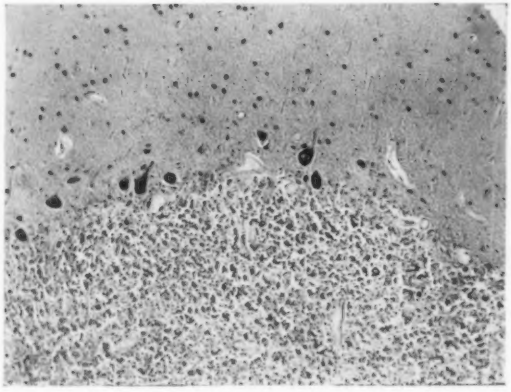

FIG. 6.

FIG. 4.—The remnants of a degenerated Purkinje cell with well-preserved basket may be noted. There are numerous fibres in the molecular and granular layers (modified Orlandi silver impregnation method, × 400).

FIG. 5.—An increase of glial fibrils in the molecular layer may be noted; definite gliosis is present in the white matter, especially around the blood-vessels. Purkinje's cells are absent and there is slight atrophy of the granular layer (Mallory's phosphotungstic acid hematoxylin, × 140).

FIG. 6.—A few of the Purkinje cells remaining. They are slightly atrophic, with few dendrites, slightly irregular in distribution, but contain normal Nissl substance. Atrophy of the molecular or granular layers is not present, and the blood-vessels are normal. There is no sign of any inflammatory process (thionin, × 115).

To illustrate Paper by Parker and Kernohan.

the meninges and blood-vessels as normal. Archambault described thickening of the meninges and blood-vessels, and emphasized these changes as being of possible causal connection.

The cerebellum therefore may be normal or atrophied to the naked eye; if atrophied the foliæ are shrivelled and the sulci widened according to a certain distribution. Microscopically, the one constant change is massive destruction of the layer of Purkinje's cells with preservation of the basket cells. Other changes are slight, inconstant and seem of little importance. Actually, therefore, the disease seems to be one in which for some reason there is specific destruction of a certain layer of cells in the cerebellar cortex and preservation of all other structures. The case reported herewith represents one more example illustrative of this specificity, and the elective affinity of the disease for the cells of Purkinje.

Report of Case.

A woman, aged 58, was brought to The Mayo Clinic, September 6, 1930, because of inability to walk. There was no history of a similar condition in her family. At the age of 28 she had had influenza and at 38 she had been confined to bed for several weeks because of nervousness and exhaustion. A diagnosis was made at that time of bronchitis. Six years before admission she had fractured her left tibia. Twenty-one months previously she had fallen for no apparent reason and fractured her left wrist. About the time that she fell she had noticed progressive weakness and exhaustion, and unsteadiness of gait. She lost weight, became nervous and was very depressed mentally. Six months previously her unsteadiness had been quite noticeable and she was sent to a hospital for a rest. She returned to work in about ten days, but her difficulties were even more marked. Four months previously she noticed that she had poor control of the use of her hands: she commenced to spill her food, writing became increasingly difficult, and finally she was unable to feed herself. She had been bedridden for three months prior to her examination at the clinic. Changes in her speech had occurred five months previously, and this had been progressive to the point where she was understood with difficulty. Her mental depression became more marked, and finally she became quite helpless.

At the time of examination the patient was pale and emaciated. She weighed 100 lb.: her normal weight was 117 lb. The systolic blood-pressure was 122, the diastolic 88 in millimetres of mercury. The pulse was 94 and during the period of eight days' observation remained about that level; there was no fever. Speech was slow and scanning. Pelvic examination disclosed a nodular, hard mass extending halfway to the umbilicus. The specific gravity of a single specimen of urine was 1·015; it was acid in reaction and contained a large number of pus cells, but no albumin or sugar. Concentration of hæmoglobin was 77 per cent. Erythrocytes numbered 4,050,000 and leucocytes 8,400 in each cubic millimetre of blood. The Wassermann test on the blood was

negative. The pupils of the eyes, the reflexes, the visual fields and the fundi were normal. Movements of the eyes were slow and incomplete, and the patient had difficulty in holding the eyes in extreme lateral rotation. There was no definite nystagmus. Roentgenograms of the thorax disclosed an old calcified apical tuberculous lesion on both sides; those of the cervical part of the spine and of the skull were negative. There was no muscular paralysis at any time and all sensations were preserved. The tendon reflexes were all active, the abdominal reflexes were preserved and Babinski's sign was not present. The finger-to-nose test and finger-to-finger test disclosed marked inco-ordination of both upper extremities, somewhat more marked on the left side. When the patient was assisted by two persons she was able to walk a few steps, swaying helplessly to either side or pitching forward. The movement of her limbs in walking was irregular, inco-ordinate and showed marked dysmetria. This inco-ordination and dysmetria were also quite marked in both upper extremities. Dysdiadokokinesia was present and marked. The Wassermann reaction of the spinal fluid was negative; the value for total protein was 20 mg. in each 100 c.c., the globulin test was positive, and there was one small lymphocyte in each cubic millimetre. The colloidal gold curve was 55444100000. The colour and the physical properties of the fluid were normal and it was under pressure of 30 c.c. of water. The pressure of the spinal fluid responded promptly to compression of the jugular veins.

The patient became steadily worse in the hospital. She vomited and became weaker. A diagnosis was made of progressive cerebellar degeneration (type unknown), bilateral calcified pulmonary tuberculosis and large pelvic tumour. She was sent home with the expectation that the terminal event would soon occur. However, she lived six months, about twenty-seven months from the presumed onset of her trouble, after her return home. She was unable to feed herself and she was practically helpless. Difficulty of speech increased, and from time to time she had attacks of fever. Ten days before death pain developed in the thorax; a friction rub could be heard and her temperature was 102° F. Necropsy was performed, and through the kindness of the pathologist the brain and spinal cord were sent to us, as well as a complete report of other findings.

The essential cause of death in this case was apparently a bilateral carcinoma of the ovary which had extended into the regional and periaortic lymph nodes. It had metastasized into the liver and lungs, and the lymph nodes of the hilum contained innumerable masses of varying sizes with necrotic centres. Evidence of extensive bronchopneumonia was present in the posterior portions of the lower lobe of both lungs. There were no findings of significance in the other organs of the thoracic and abdominal cavities.

The brain and spinal cord had been removed intact and reached us in excellent condition in solution of formaldehyde. To the naked eye

no lesions of any part of the nervous system were apparent. There was no atrophy of the cerebellum and the foliæ seemed to be of normal size (Plate VI, fig. 1). There was no arteriosclerosis of the vessels of the circle of Willis or of any other vessels. The meninges were not thickened, nor was there any turbidity. The cerebrum was cut by coronal sections but evidence was not found of hydrocephalus, infarcts, or metastatic tumours. The mid-brain, pons and medulla appeared normal.

Sections were taken from all parts of the nervous system, including cerebrum, cerebellum, brain-stem and spinal cord and also the meninges. The stains used on these sections were Weigert myelin sheath, hæmatoxylin and eosin, thionin and the Orlandi modification of Bielschowsky silver impregnation method. Since the brain had been fixed in solution of formaldehyde, the gold chloride and sublimate method of Cajal and the silver carbonate method of Rio Hortega could not be carried out, and Mallory's phosphotungstic acid hæmatoxylin stain was used for glial fibrils.

Microscopically the various sections disclosed: (1) The meninges and blood-vessels were normal. (2) An excess of lipochrome pigment was noted in the anterior horn cells of the spinal cord, but there was no degeneration in these cells. There was no degeneration of any of the tracts and sclerotic plaques were absent. (3) There were no changes in the axis-cylinders, myelin sheaths or glial cells of the medulla oblongata, pons and mid-brain. In the olivary nuclei of the medulla oblongata there was an excess of pigment in many of the ganglion cells which were otherwise normal. The pigment was usually in the form of minute granules, but they were sometimes quite large. All had an affinity for silver but did not react specifically for iron. Weigert's myelin sheath stain did not show degeneration in any of the tracts of the medulla and brain-stem, including the olivary connections. There were several small groups of vacuoles near the olivary nuclei, the nature of which could not be accurately determined. There were no findings indicating inflammatory reaction. (4) Sections were taken from various portions of the cerebral cortex; there was no chromatolysis or pyknosis of any of the ganglion cells, but many of the larger pyramidal cells contained an excess of pigment which had an affinity for thionin stain and for silver. This was more marked, however, in the cells of the basal nuclei, where every cell contained pigment, but again there was no other sign of degeneration. (5) Microscopical preparations were made from numerous areas of both cerebellar hemispheres, the vermis and dentate nuclei. The outstanding condition was diffuse destruction of the

Purkinje cells with preservation of the basket cells. Sections taken from the different portions of the cerebellar hemispheres and vermis were examined separately and the findings compared.

In the inferior border of the left hemisphere the hæmatoxylin and eosin stain did not disclose signs of old or recent meningitis or any inflammatory condition, and no scavenger cells or evidences of phagocytosis were noted. In the molecular layer there appeared to be a slight increase of cells in scattered foci, but this increase was not general. Many of the nuclei of these cells seemed to be astrocytes, but some were large and vesicular with a deeply staining central nucleolus. The molecular layer was of normal thickness and was neither atrophic nor hypertrophic. There was no pigment and no rarefaction of the tissues in this zone. There was no decrease or increase in the number of cells in the granular layer so that it was neither atrophic nor hypertrophic although the nerve-fibre layer was normal. With the thionin stain those cells in the molecular layer which had large vesicular nuclei, and deeply staining nucleoli were seen to be very small ganglion cells. There was a narrow ring of cytoplasm, containing numerous fine granules of Nissl substance surrounding the nuclei (Plate VI, fig. 2). These cells did not have any dendrons and most of them were rounded, although occasionally the Nissl granules collected into several masses giving the cells a pyramidal or polygonal shape. None of these cells was bipolar, and all seemed to be differentiated and mature. In the Purkinje cell layer all ganglion cells had disappeared although occasional faint traces of degenerating ones were visible. Pyknotic cells were not present. There were no small ganglion cells similar to those seen in the molecular layer. All the cells of the granular layer were normal, except some small ganglion cells similar to those seen in the molecular layer. These were scattered throughout the granular layer but were more common near the Purkinje cell layer. There were no large ganglion cells like Purkinje cells in the layer. With the Orlandi modification of the Bielschowsky impregnation method the small ganglion cells in the molecular layer did not have dendrites or axis-cylinders, although they did have an affinity for silver. In the deeper part of the molecular layer, there were many normal axis-cylinders lying parallel to the surface of the convolutions; these were not beaded or fragmented. Close to the Purkinje cell layer there were some very fine axis-cylinders projecting into the molecular layer; these belonged to the processes of the basket cells. Although the Purkinje cells had disappeared leaving no trace practically all the baskets surrounding the disintegrated Purkinje

cells were intact. In spite of the complete absence of normal Purkinje cells and their processes, the surrounding basket fibres were intact and normal (Plates VI and VII, figs. 3 and 4) with numerous processes and fibrils just as if the Purkinje cells were present. All the baskets were intact, but some were better seen than others. There were innumerable axis-cylinders running in all directions in the granular layer and some entered the nerve-fibre layer. All the axis-cylinders of the granular layer and the nerve-fibre layer were normal; there was no apparent diminution in numbers, and there was no degeneration. The axis-cylinders in the nerve-fibre layer were parallel to each other, and there was absence of beading, swelling and fragmentation. Mallory's phosphotungstic acid hæmatoxylin stain showed that there were many neuroglial fibrils running at right angles to the pia mater in the outer two-thirds of the molecular layer. The inner third was devoid of such gliosis. Most of the Purkinje cell layer was also devoid of glial fibrils, although occasionally small clusters were present. There were more fibrous astrocytes in the granular layer than normal, and there was a marked gliosis in the nerve-fibre layer. This formed a denser mat than is normal and was pronounced around the blood-vessels, especially around the large vessels (Plate VII, fig. 5).

In the lateral portions of the left hemisphere findings similar to the foregoing were present in the molecular layer, and a smaller number of similar cells were present in the superficial part of the granular layer. There was a slight increase in the astrocytes in the molecular layer. There was no rarefaction in the Purkinje cell-layer, and no Purkinje cells were present in the molecular or granular layers. All the other tissues were normal. There was no old or recent inflammation in any of the layers of this part of the cerebellum.

In the superior border of the left cerebellar hemisphere, findings were also similar to those of the inferior and lateral borders, except that some Purkinje cells were undergoing chromatolysis. No normal cells were found. In the molecular and granular layers close to the remnants of the Purkinje cells there were fewer small ganglion cells. Axis-cylinders undergoing active degeneration were not found. In the inferior and lateral borders of the right hemisphere there was complete absence of Purkinje's cells and the other findings were identical with those of the left hemisphere. However, in the superior border of the right hemisphere close to the vermis there was a considerable number of well-preserved Purkinje's cells. In several foliæ there were Purkinje's cells, normal both in numbers and structure except that an occasional cell was

out of alignment and was situated in the lower third of the molecular layer. The other layers of the cerebellum, superficial and deep to these cells, were normal. In the outer portions of several foliæ there were normal Purkinje cells, and in the deeper recesses of the foliæ they had completely disappeared. The transition between these two portions was abrupt (Plate VII, fig. 6). There was no demonstrable reason for the abrupt change; the blood-vessels in each portion were normal, there was no sign of old or recent inflammation, and the other layers of the foliæ were normal. The baskets were present and equally well preserved in both portions. In such folia there were no small ganglion cells in the molecular or granular layers, but there seemed to be a slight increase in the number of glial cells in the molecular layer.

The inferior vermis was similar to the other portions of the cerebellum, and the Purkinje cells were absent. The only difference was an increase in the number of small ganglion cells which were more numerous in, and scattered diffusely through, the granular layer.

The superior vermis was similar to the inferior vermis, except that occasional normal Purkinje cells were present. Several small areas (portions of several folia) retained normal Purkinje cells which seemed to survive in small segments of the foliæ, and the junction with their adjacent portions where the ganglion cells had disappeared was abrupt.

The ganglion cells of the dentate nuclei were intact, but most of these cells contained excessive pigment which was frequently collected into coarse granules and had an affinity for silver, but did not react specifically for iron. Some cells had disintegrated, as occasional granules of this pigment were lying free in the stroma or in the perivascular spaces. Cells were not undergoing chromatolysis, but an occasional cell appeared to be pyknotic. There was a zone of rarefaction surrounding both dentate nuclei which appeared spongy. The vacuoles seemed to be the result of numerous swollen oligodendroglial cells. Besides this zone of rarefaction there was an excess of astrocytes which was most marked in the hilum of the dentate nuclei. Mallory's phosphotungstic acid hæmatoxylin stain showed that most of the astrocytes were of the fibrous type, with numerous neuroglial fibrillæ. There was no sign of recent or old inflammation in or around the dentate nuclei. Weigert's myelin sheath stains did not show degeneration of the myelin around the nucleus even where the zone of rarefaction was noted.

The blood-vessels in all parts of the cerebellum were normal. There was no evidence of arteriosclerosis, and the perivascular spaces were not dilated, and no cells or products of degeneration were present.

Comment.

Clinically the case recorded here is comparable with cases reviewed in the literature. The onset of the disease was insidious, as is usually the case. The patient dated her troubles from the time when she fell and fractured her wrist. It is probable that her balance was not quite normal at the time. Her age was about 56 when symptoms commenced; about the average age when the disease usually commences. The course was unusually short, lasting only twenty-seven months, in contrast to the more chronic cases reported. Complete helplessness was reached within a few months; the case therefore resembles the single case of Murri in which the disease ran its complete course from onset to death in eight months. There was no dissociation between involvement of lower extremities and the disturbance in the upper extremities. The ataxia and inco-ordination were universal and involved the movements required for articulation also. In six of the total twelve cases the patients were similarly affected, thus in 50 per cent. of the cases the disturbance of the upper extremities approximated that of the lower extremities.

As usual there was no nystagmus, suggesting clinically a lesion confined to the cerebellum and leaving the vestibular nuclei or their corresponding tracts in the brain-stem intact. There was nothing of the violent movement tremor seen in multiple sclerosis, and the sphincters were unaffected. As is usual also, the patient's intelligence was unimpaired.

In considering the diagnosis in this case there were some extraneous factors that finally turned out to be more associated than causal. The patient had an old pulmonary tuberculous lesion, and a pelvic tumour of uncertain nature. Tuberculoma of the cerebellum or metastatic carcinoma to the brain was considered, but finally rejected because of lack of corroborative evidence. Nevertheless, they were the confusing details of the clinical findings. Multiple sclerosis was also considered as is so often the case in these diseases, but was rejected because of the age of the patient and the purity of the cerebellar syndrome. Finally, no other conclusion could be reached than that the disease was a progressive degenerative process in the cerebellum.

With regard to the influence of the carcinoma on the disease, one can only assume that in the main it constituted a terminal event; it is possible that the cachexia and weakness resulting from it exaggerated the general functional impairment and helplessness. The disease comes

on at a time in life when the incidence of carcinomatous changes is high and at least one other patient, described by Lhermitte, suffered similarly from carcinoma of the pancreas that caused death. Like the pulmonary tuberculosis, the carcinoma probably had no causal connection, although it made the diagnosis more difficult.

If our case resembled in its main clinical features the characteristics of the cases reported in the literature, the resemblance in pathological detail was much more close. As always, the predominant feature was the diffuse and massive destruction of the Purkinje cells with preservation of the basket cells. It is true there was no gross atrophy and the disease in question has been called cerebellar atrophy. Nevertheless, in a case of Marie, Foix and Alajouanine and in the case of Jelgersma, the cerebellum was normal in size. This, however, does not preclude atrophy which is cellular and specific for one type of cell, and at the same time is unassociated with diminution of the gross volume of the cerebellum. It is possible that a more slowly progressive process causes greater shrinkage in size due to secondary sclerotic processes. Nevertheless, Jelgersma's patient had the disease eight years before death. Similar to the other cases there were no striking changes elsewhere in the nervous system, as the various tracts connecting the cerebellum with other structures were entirely normal. Some minor changes were observed, and for the sake of completeness will be given some consideration.

The diffuse pigmentary change in many of the ganglion cells throughout the central nervous system must be considered abnormal. With advancing age there is normally an increase of lipochrome pigment in many ganglion cells and frequently in most of them, but in this case it was in excess of that usually seen in persons of an age similar to this patient. The significance of an excess of pigment is unknown, but the consensus of opinion considers it a sign of wear and tear or a degenerative phenomenon, but there is no evidence to suggest that the presence of this melanin-containing pigment interferes with the function of the cell. Usually the pigment granules are minute and the melanin portion has an affinity for silver, as was noted in this case, whereas the lipoid part has an affinity for fat stains and the pigment gives a polychrome reaction with thionin. In some cells, especially in the dentate nucleus, the small granules had fused into larger ones, which could readily be seen with a lower power microscope, and occasionally there were free granules indicating complete disintegration of the cells. These granules were free in the glial spaces and occasionally in the perivascular spaces,

but there was no evidence that phagocytosis had taken place, and there was no activity of the microglial or other scavenger cells.

There was absence of any general glial reaction, and that around the dentate nuclei was sharply localized for which there is no satisfactory explanation. It could scarcely be a post-mortem phenomenon on account of its sharp demarcation, and there was not sufficient degeneration of the ganglion cells to account for the reaction of the oligodendroglia or the astrocytes. The pigmentary degeneration of the ganglion cells of the dentate nuclei was more advanced than that observed in any other group of cells in the central nervous system, and this may be the result of the disappearance of the Purkinje cells. The similar but less severe changes in the ganglion cells of the olivary nuclei may be accounted for on the same basis. In spite of the pigmentary changes the ganglion cells of both the dentate and olivary nuclei had retained their functions as the axis-cylinders and their accompanying myelin sheaths were intact.

The disease from which the patient died has been referred to as cerebellar atrophy, yet in most cases, and in our case in particular, there was no gross evidence of atrophy, and the degeneration was sharply limited to the Purkinje-cell layer, and practically all the other changes noted microscopically were secondary to this. The presence of very small and apparently immature ganglion cells in the molecular and granular layers might be interpreted as an attempt at regeneration or formation of new cells to replace the Purkinje cells that were destroyed. If this is the explanation of the presence of these small cells, such a phenomenon is unique in the central nervous system. The slight increase of astrocytes in the Purkinje-cell layer should be regarded as a replacement phenomenon and we did not consider it the primary lesion. Altogether the changes found under the microscope and apart from the destruction of the Purkinje cells seemed unimportant and could hardly have led to any marked impairment of function.

General Comment.

So far, we have considered the results of observation and have dealt with facts. Proceeding thence to hypotheses as to the causation of the disease, we are treading on much less certain ground. The uncertainty lies in the lack of uniformity of antecedent phenomena in the disease. Marie, Foix and Alajouanine had covered all the possible ætiological factors up to the time of their publication. They emphasized two main factors, namely an early infectious process antedating the appearance of

the disease, and its late onset in the life of the patient. They invoked a double pathogenesis, and suggested that a previous infection or toxic process had injured a poorly endowed Purkinje-cell system leading later to premature decay. The element of infection or intoxication is necessary as well as an abiotrophic condition of the cell. Archambault also suggested an antecedent infectious process as cause, but it acted on the meningeal vessels and determined a slowly progressive atresia of these cells leading in later life to cortical atrophy from malnutrition. Unfortunately for this latter hypothesis, the majority of observers has failed to find significant lesions in the vascular system supplying the cerebellar cortex.

If an infectious origin is assumed, the case of Murri showed a fair basis for this hypothesis. The disease began with severe gastro-enteritis which persisted during most of the subsequent events, and the patient died after being ill only eight months. Symptoms developed in a case of Rossi fifteen days after the patient had had severe diarrhœa that persisted for six weeks. This patient died of cirrhosis of the liver. Stender and Lüthy, however, were satisfied that chronic alcoholism was the main cause, and certainly they had reason, as the patient had had delirium tremens three times and his cerebellar difficulties commenced following severe neuritis caused by alcohol. Kirschbaum and Eichholz also believed alcoholic excesses were to blame, for though the patient had never indulged, for three generations his family had been heavy drinkers of alcohol. It was assumed that this heritage led to a system poorly endowed with Purkinje cells, so that at the age of 20 spontaneous degeneration developed and continued until the patient's death. Thomas's patient had had syphilis, alcoholism, typhoid fever, otitis media and probably acute anterior poliomyelitis. So many antecedent illnesses make the problem here too complex for direct argument as to cause and effect.

Unfortunately, there is a negative side to the picture. There is an appreciable number of cases on record, including those of Jelgersma and Lhermitte, in which the past history of the patient gave no indications of infection or intoxication. Our patient had had influenza thirty years before the onset of her symptoms, but it was not particularly severe and was merely mentioned when the history was being taken. Anyone reaching an age between 50 and 70 years had a good chance of having had at some time in life some type of mild or severe infection. To associate this with a disease appearing many years later required a large amount of proof. Nevertheless, exceptions to this can be found in other

diseases of the nervous system as will be mentioned. To presume that a patient is constitutionally predisposed to a disease without a familial or hereditary history of the disease is also begging the question. It may be necessary to approach the problem from a different angle.

Since the outstanding feature of the disease is a progressive selective deterioration of the Purkinje cells and relative conservation of the other elements in the cerebellum, it might be asked whether there is any reason for assuming that the cells are particularly weak in middle age and later. There are some observations tending to support this assumption. The Purkinje cells are present at birth but underdeveloped and immature in form. There is then rapid growth during the first six months, but they do not reach full size until from twelve to eighteen months after birth. Later acquired structures in the central nervous system are usually the first to disappear during senescence and disease. Ellis found that there is a gradual loss of Purkinje cells with advancing age. This begins normally at about the age of 40 and gradually progresses as time goes on. As well as actual disappearance of cells, degenerative changes also occur in those that remain; chromatolysis, atrophy, vacuolation and homogenous degeneration of the nucleus and cytoplasm and pigmentary changes were found in the Purkinje cells of old age. Moreover, the regions most affected were those most injured in cortical cerebellar atrophy. The cells of the dentate nucleus were much less affected in senescence. Inuka found the same senile degeneration of the Purkinje cells in albino rats, but not to the same degree as in human beings.

The progressive changes in the Purkinje cells that occur after the age of 40 might indicate a relatively increased vulnerability of these cells as compared with other portions of the cerebellum, more especially in later life. The question also arises as to whether in the more well-known types of progressive cerebellar atrophy occurring just before or after middle age, the Purkinje cells are badly affected. This is actually the case in the olivo-ponto-cerebellar atrophy described by Dejerine and Thomas, the olivo-rubro-cerebellar atrophy of Lejonne and Lhermitte, and particularly in the type of familial degeneration of the cerebellum described by Holmes. In the latter disease the Purkinje cells of practically the whole cortex except the tonsils, the uvula and the nodule are severely affected, and this destruction of Purkinje's cells is the most conspicuous change in the cerebellar cortex. Again a local selectivity of disease appears, in that the degeneration of the Purkinje cells is most severe in the superior vermis, the flocculus and the pyramid. In these

types of cerebellar degeneration of adult life other structures are badly injured, but the Purkinje cells receive more than their share of injury. Accordingly, the thesis might be advanced that in adult life, especially after the fifth decade, the Purkinje cells are more readily affected by age and disease than the rest of the cerebellum, and have a relatively high degree of vulnerability.

From the standpoint of histological changes the disease in question might represent the influence of endogenous or exogenous toxins, of some unknown type of disease or so-called degeneration as yet not understood. There is no evidence of acute or chronic inflammation, although such may have at one time appeared and disappeared without leaving a trace of its previous existence. Inorganic toxins such as lead have been known to injure the Purkinje cells, as the experimental work of Ferraro and Hernandez has shown, but this injury is not specific for the cells and exerts its influence elsewhere in the nervous system. Alcohol has been suggested by Stender and Lüthy as the essential cause in their case. Considering the common use of alcohol there ought to be a higher incidence of the disease, but actually it is quite rare. An endogenous toxin is an improbable cause, since there is no obvious source for it and no indication of its action elsewhere in the body. To call the condition a degenerative disease opens the question as to what caused the degeneration.

Recently, attention has been drawn to the problem of changes of tissue in virus diseases, notably by Ledingham. Acute types, such as acute anterior poliomyelitis, are well known, but as yet our knowledge of chronic forms of such disease is limited. Cases have been recorded of chronic disease of the anterior horn cell commencing anew and progressing to a fatal termination years after an episode of acute anterior poliomyelitis was over. Oppenheim described clinically a chronic anterior poliomyelitis that may appear without any antecedent history of infection. Homologous to this is chronic bulbar palsy, in which the cells of the motor nuclei of the bulb disintegrate. These diseases, moreover, are more prone to occur in the later decades of life. At necropsy little is found outside of the specific destruction of cells. Epidemic encephalitis may be followed by a chronic progressive Parkinsonism which may appear ten years or more after an initial encephalitis and progress to a fatal termination. Of recent years cases of this chronic disease have been observed in which there is no history of epidemic encephalitis, or perhaps of mild influenza or a common cold. In some of the chronic cases no change is found after death other than

progressive destruction of the cells of the basal ganglia and substantia nigra. All evidence of acute or chronic encephalitis had disappeared long since. It is, therefore, not impossible that parenchymatous cortical cerebellar atrophy is in some instances at least due to a virus disease. It may be introduced into the body during some previous infection, lie dormant throughout the years, and then fasten on to the Purkinje cells at an age when they are least resistant. Thus is started a slow, remorselessly progressive disease, ending in helplessness and death.

Support for these ideas as to causation would be manifest if there existed an acute specific disease of Purkinje's cells of virus origin, as occurs in the anterior horn cells of the spinal cord. In human beings such a condition is of extremely rare occurrence. There is, however, an acute virus disease affecting animals and destroying specifically the Purkinje cells. This disease occurs in epidemic form in sheep, and is confined apparently to some counties in the north of England. It has been called "louping-ill" and is transmissible to mice and monkeys [2, 6]. Hurst produced the disease in four monkeys, and it was characterized by progressive cerebellar ataxia. At necropsy, a more or less diffuse encephalomyelitis was present, accompanied by massive destruction of the Purkinje cells of the cerebellum. Hurst drew attention to the analogy between this disease and acute anterior poliomyelitis.

In the final analysis as to the cause of the disease in the group studied, it is probable that more than one factor is to blame. Chronic alcoholism may be the cause in one group of patients. Among patients whose difficulties are beginning at an advanced age, premature senescence of the Purkinje cells might be suggested, especially as it is known these cells tend to decay in advance of other cells. Among younger patients with a history of somewhat more rapid onset, and with an antecedent or parallel infectious or toxic process, a virus disease with a specific affinity for the Purkinje cells might be considered. Finally, as is usually the case, there may be a group of cases in which clues as to the essential cause are lacking and the ætiology is unknown.

Summary and Conclusions.

The clinical and pathological characteristics of parenchymatous cortical cerebellar atrophy have been outlined. Hypotheses have been expressed as to the cause of the disease. The histological findings at necropsy are characteristic, and readily recognizable. Clinically, the

SUMMARY OF DATA

Author and year	Age, years and sex	Duration of disease years	Previous illness	Involvement	Tremor	Speech	Cause of death	Gross appearance of cerebellum	Comment
Murri 1900	59 F.	¾	Gastro-enteritis	General	Hands	Slow, hesitating	Cardiac failure	Not mentioned	Rapid course
Thomas.. .. 1905	40 F.	19	Typhoid, syphilis, alcoholism; anterior poliomyelitis	Trunk and lower extremities	Lower extremities	Nasal (gumma of palate)	Chronic bronchitis	Normal	Claw feet; extensor plantar reflexes, spastic toward end
Rossi 1907	59 M.	9	Diarrhœa	Lower extremities	Hands	Spasmodic	Cirrhosis of liver	Atrophied	
Archambault .. 1918	17 M.	18	Typhoid	General	Head and extremities	Slow, monotonous nasal	Pneumonia	Atrophied; reduced by ⅓	Some rigidity legs and arms; early onset
Jelgersma .. 1919	80 M.	8	None	General	Head and arms	Slow, explosive	Not mentioned	Normal	
Lhermitte .. 1922	67 M.	13	None	Lower extremities	None	Not mentioned	Carcinoma of pancreas	Atrophied	
Marie, Foix and Alajouanine 1922	68 ?	14	None	Lower extremities	None	Slow	Not mentioned	Atrophied; reduced by ⅓	
Marie, Foix and Alajouanine 1922	62 ?	6	None	Trunk and lower extremities	None	Normal	Not mentioned	Atrophied; reduced by ⅓	
Marie, Foix and Alajouanine 1922	60 M.	5	Unimportant	Trunk and lower extremities	Lower extremities	Drawling, monotonous	Not mentioned	Atrophied	
Stender and Lüthy 1931	60 M.	10	Chronic alcoholism; delirium tremens; alcoholic polyneuritis	General	Arms	Monotonous; indistinct; ataxic	Bronchopneumonia; senility	Atrophied	
Kirschbaum and Eichholz 1932	20 M.	39	Acute rheumatic fever	General	Arms	Staccato, slow, indistinct	Apoplexy; pneumonia	Atrophied	Early onset
Parker and Kernohan 1933	58 F	2	Influenza	General	None	Slow; scanning	Carcinoma of ovary	Normal	Rapid course

disease represents a slowly progressive cerebellar syndrome, beginning after middle age in both men and women. The diagnosis need not be very difficult except when separating the clinical syndrome from other types of cerebellar degeneration. The failure to obtain a history of heredofamilial characteristics and the relative purity of the cerebellar syndrome are of assistance in the latter respect. Arteriosclerosis with infarction of the cerebellum produces a clinical course that is abrupt and intermittent, and lacking the smooth progressive course of the disease outlined. The disease usually begins before senile changes are manifest, and the preservation of the intellectual faculties distinguishes it from a general senile breakdown of the nervous system.

The disease is rare; only twelve cases, including our own, have been recorded in which necropsy has verified the identity of the process. Interest in the condition is created by the observation of a clear-cut clinical syndrome and a specific destruction of cells in the cerebellum. We hope that this study will lead to a better understanding of the mechanism that underlies not only the physiologic reactions to disturbed cerebellar structure, but to the factors involved in cellular pathologic changes.

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THE LOCALIZING SIGNIFICANCE OF SPASTICITY, REFLEX GRASPING, AND THE SIGNS OF BABINSKI AND ROSSOLIMO.

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In Babinski's original description [1] of the pathological plantar reflex published in 1896, he stated that the reaction consisted of simple extension of the toes. In 1903, however, he observed [2] a second component of the response, *i.e.*, fanning and lateral deviation of the toes, which "in certain cases," especially in familial diplegias, accompanied the simple extensor reaction. Since then the extensor phenomenon has been clearly established as pathognomonic of pyramidal tract lesions, but the significance of the fanning sign in relation to localization has not, so far as we are aware, been given serious consideration. Fulton and Keller [10] in their study of the Babinski response in chimpanzees observed fanning in several instances following lesions of motor projection areas of the cortex, and more recent observations, which we propose now to record, indicate that the phenomenon is not associated with lesions of the pyramidal tracts.

The present study is based largely upon the chimpanzee, and in particular upon four tame specimens in which various cortical lesions were made. Corroborative evidence drawn from the monkey, baboon and gibbon, has been included where relevant, but these forms are less well suited for the problem in hand since they exhibit fewer of the common pathological reflexes of clinical significance (Fulton and Keller [10]; Schick [20]).

The "Motor" Areas of the Cortex.

Cortical lesions restricted to Area 4 of Brodman [4, 5], *i.e.*, to the classical motor area from which the pyramidal tracts take origin (fig. 1), give rise in the chimpanzee and apparently in all other primates, to a simple, and for the time being complete, *flaccid* paralysis [10, 11]. Within a few weeks after such a lesion, however, the animal recovers volitional power in all muscles except those governing the finer move-

ments of the digits. Spasticity has never been seen in the affected extremities following such an extirpation, except as a transient phenomenon in a few instances.

When the premotor area (Area 6 of Brodman) is destroyed (fig. 1) in primates a different picture is seen, *i.e.*, there is transient loss of voluntary power in the contralateral extremities [14, 6], but the paresis is accompanied by an increased resistance to passive manipulation, and

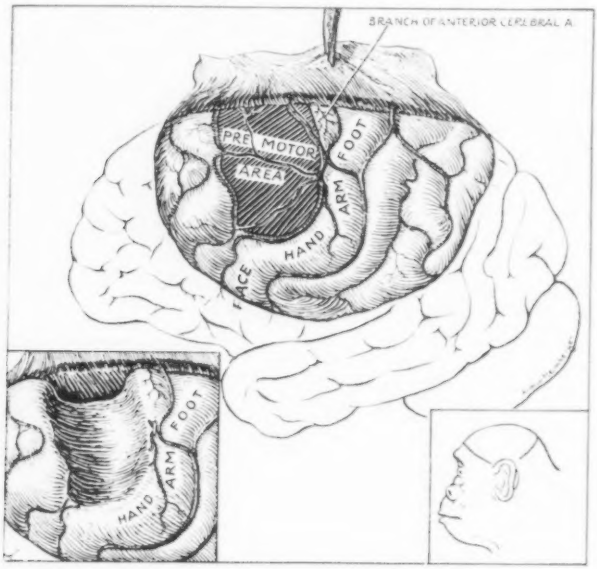

FIG. 1.—Left hemisphere of a chimpanzee (Experiment 4) showing the motor cortex (Area 4) from which the arm area was extirpated April 19, 1932, and the premotor cortex (Area 6) extirpated November 11, 1932.

the limbs become *spastic* [10]. In addition, involuntarily reflex grasping occurs, as was first demonstrated experimentally by Richter and Hines [17, 18] (see also [9]). Both these phenomena disappear, usually in a few days, and the ultimate motor performance of both the monkeys and chimpanzees is on the whole normal, though a curious reluctance to initiate voluntary movements may persist indefinitely [14].

If, from a chimpanzee in which Area 4 has been destroyed,[1] the pre-

[1] Full details concerning the results in monkeys of successive removal of Areas 4 and 6 from both hemispheres in various combinations have been reported by the present authors in another paper [11, 12].

motor region of the same side is removed at a second operation, the opposite extremities again lose voluntary power completely, and become immediately *spastic*, exhibiting lengthening and shortening reactions, the "clasp-knife" phenomenon, &c. Recovery of voluntary power in the small muscles of the digits does not occur, though gross flexion and extension movements of the larger joints may be regained, the ultimate residual deficit is far greater in all muscles than that which follows isolated extirpation of Area 4 or Area 6 alone [11]. The spasticity and correspondingly greater motor deficit also occur when Areas 4 and 6 are removed simultaneously. It is evident, therefore, that the presence of spasticity, in the chimpanzee, and probably in man, has definite localizing value in the study of cortical lesions, especially when considered in relation to the pathological reflexes discussed below.

Experimental Material.

The four animals on which the study is based may now be briefly described. All surgical procedures were carried out under sodium amytal anæsthesia, except for the fourth operation in Experiment 4 in which ether was used. For each operation a bone flap was turned down and ultimately replaced with all precautions that one ordinarily employs for a similar operation on man. (See Fulton and Keller [10].)

A detailed study of pathological reflexes other than the Babinski in various primate forms has been made recently in this laboratory by Schick [20] who has established in the chimpanzee the responses homologous with the signs of Chaddock, Oppenheim, Schaffer, Gordon, Rossolimo and Mendel-Bechterew in man. For elicitation of these responses in chimpanzees we have followed the procedures which he has described. Attention may be directed again to the fact that the signs of Rossolimo and Mendel-Bechterew which are exaggerated "deep" reflexes, *i.e.*, tendon responses of the digits, fall into a group quite separate from the cutaneous Babinski, Chaddock and Oppenheim responses. Flicking the tips of the toes, or tapping the digital tendons near the metacarpophalangeal joints serve as the adequate stimulus for the Rossolimo reflex [19].

Experiment 1 ("*Yama*"). *Male chimpanzee weighing* 17,300 *grm. Successive removal of Area* 4 (*foot*) *from both hemispheres at intervals of six weeks followed in each instance by flaccid paralysis and Babinski response without fanning. Subsequent removal nine months later of Area* 6 (*left*),

[1] Weights indicated in these four experiments are as of April, 1933.

followed by strong contralateral spasticity, loss of voluntary power, forced grasping, pronounced and permanent Rossolimo's sign and the fanning sign of Babinski.

The subject of the experiment was a well-trained and co-operative chimpanzee, the early history of which has been fully described elsewhere (Fulton and Keller [10], Experiment 16). The foot areas were identified by faradic stimulation and removed, one on January 21, 1932 (left) and the other on March 4, 1932. In each instance the lesion, restricted to Area 4, gave rise to a striking flaccid paralysis of the opposite hind limb with depression of deep and superficial reflexes for a period of several days after each operation. The Babinski phenomenon was at first sluggish, but it increased gradually in

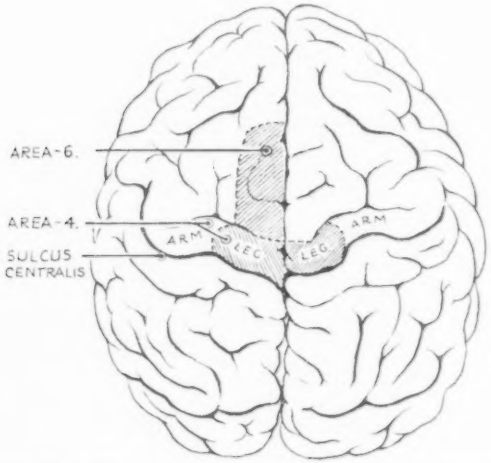

FIG. 2.—Drawing of the cerebral hemispheres of a chimpanzee (Experiment 1) showing the left motor foot area extirpated January 21, 1932, the right motor foot area extirpated March 4, 1932, and the left superior premotor area extirpated December 6, 1932.

amplitude during the first week, and after the second operation ultimately became equal on the two sides and readily obtained. For a period of eight months thereafter it remained constant. The response was unassociated with the fanning sign of Babinski, and the signs of Rossolimo and Mendel-Bechterew, though present immediately after the operation, were never marked. Forced grasping could not be evoked. The gradual return of voluntary power in all muscles, except the digits, has been previously described [10].

Removal of left premotor area.—On December 6, 1932, the superior part of the left premotor area was removed under sodium amytal anæsthesia (fig. 2). On recovery from anæsthesia the animal had a markedly spastic right hind limb which within less than forty-eight hours began to show: (1) The fanning sign of Babinski with great increase in the ease of elicitation of the sign of

Babinski itself; (2) involuntary forced grasping of hand and foot—that of the hand passed off after ten days, but in the foot, provided the body was in the maximal position for the grasp reflex (see Bieber and Fulton [3]), it could still be demonstrated at the end of four months; (3) a pronounced Rossolimo response obtainable with a slight stimulus. The spasticity and impairment of motor power diminished somewhat after six weeks, but the fanning, forced grasping and a pronounced Rossolimo reaction have persisted (four months), and bid fair to be permanent. At present (April, 1933), the animal shows the following signs: In the right lower extremity a positive Babinski, Chaddock, Rossolimo, Mendel-Bechterew and a general motor deficit which is markedly accentuated by fatigue. There is also slight spasticity and forced grasping and the fanning sign of Babinski which is not present in the left foot. On the left, the Babinski and Rossolimo are positive, but less easy to elicit and less well marked than on the right. There is no forced grasping or spasticity, and motor function on the left is far better than that on the right.

Experiment 2 ("*Boy*"). *Young male chimpanzee weighing* 13,600 *grm. Successive removal of Area* 6 *from both hemispheres, followed in each case by forced grasping, transient spastic paresis, marked impairment of spontaneous motor performance and permanent Rossolimo with modified fanning sign, but absent Babinski.*

This animal, a young and tame male chimpanzee, has been trained by Dr. C. F. Jacobsen in problems [14] requiring skilled movements of the hands and fingers. On December 9, 1932, the left premotor area (Area 6) was removed. Forced grasping immediately became prominent in both right extremities and persisted for about ten days, gradually disappearing as voluntary prehension returned to hand and foot. With the forced grasping there was an increase in resistance to passive manipulation of the right extremities, and a state of spasticity which appeared to cause the right extremities to be moved slowly and less readily than the left, and to be held in a characteristic semi-flexed posture when the animal was at rest. During the first two days after operation a jerking extensor response to plantar stimulation occurred on the right and was accompanied by a flaring of the smaller toes. After the second day, this response was always flexor in type and was accompanied by lateral deviation of the toes. The sign of Rossolimo was elicitable in the right at first but disappeared after two weeks. The right knee-jerk was more active than the left, immediately following operation.

At a *second operation* (January 9, 1933), Area 6 was extirpated from the right side. Immediately following the operation, the *right* extremities became markedly *spastic*; the left were flaccid during the first post-operative day, but then became very spastic also. Extreme spasticity was present for nearly two weeks, but after this it gradually became less and disappeared at the end of the third week. During the first weeks forced grasping was present in all four extremities, disappearing gradually as the spasticity became less and persisting longer in the hands than in the feet.

The plantar reflexes again became extensor in type on both sides during the first post-operative day, but exaggerated plantar flexion supervened on the second day and has persisted three months, associated with the fanning sign, *i.e.*, there is lateral deviation of the toes in addition to the flexion response. The deep reflexes, *i.e.*, knee-jerks, were exaggerated. The Rossolimo reflex returned on the right in more pronounced form and it also appeared on the left, and has persisted permanently on both sides.

At present (April, 1933), no motor deficit can be detected and the performance of the animal appears normal, but the knee-jerks continue hyperactive and the Rossolimo sign, although less marked, is still easy to elicit bilaterally. The plantar responses are exaggerated flexor in type on the right but they have become variable and difficult to elicit on the left side.

Experiment 3 ("*Sambo.*")—*Mature male chimpanzee weighing* 38,000 *grm. Radical removal of entire premotor area from left hemisphere, followed by spasticity, forced grasping, signs of Rossolimo and fanning and transient Babinski.*

The animal had been in the laboratory for six months and had also been trained on problem boxes. On January 3, 1933, the entire left premotor area was removed (fig. 1), the excision being deeper and more radical than in Experiment 2, but it did not impinge on Area 4. A profound right motor deficit ensued with extreme spasticity and forced grasping which still persisted after six weeks, although it had gradually become less pronounced.

An extensor Babinski response was present on the right side during the first eight days, and was accompanied by a flaring and lateral deviation of the digits which has persisted but the extensor response of the digits has disappeared. The Rossolimo sign was observed to be positive on the sixth post-operative day and has persisted in well-marked form for three months.

Subsequently (April 24, 1933) the right premotor area was also removed which caused re-appearance of forced grasping on both sides and the Rossolimo sign was permanent on both sides. At a third operation on June 2, the entire motor area above the face was destroyed on the left side, after which the extremities became highly spastic and have remained in this condition until the present time (July, 1933).

Experiment 4 ("*Mussai*").—*Male chimpanzee weighing* 24,200 *grm. Removal of both arm areas (Area* 4*) and both premotor areas (Area* 6 *entire) at four successive operations. Permanent forced grasping in arms. Permanent Rossolimo and transient fanning of toes, but no Babinski.*

The subject of this experiment was a young male chimpanzee which had been trained on box problems during a period of eight months prior to its first operation. On April 19, 1932, the left motor cortex representing the arm was removed, and on May 15, 1932, the corresponding area was removed from the right motor cortex. After each operation, flaccid paralysis of the contralateral arm occurred followed by gradual recovery of function, but with permanent impairment of movements of the digits. There was no impairment

of motor function of either lower extremity. After the first operation a slight and transient Rossolimo appeared in the right foot, but disappeared completely on the eighth post-operative day.

No other pathological reflexes of the lower extremities were demonstrated until the *third operation* (November 11, 1932) when the entire *left* premotor area was removed (fig. 3). Spasticity of the right arm with very marked forced grasping of that hand appeared at once and both symptoms persisted, although in recent months they have tended to become slightly less pronounced. Very slight and transient spasticity of the right leg was also evident, with slight involuntary groping and grasping which disappeared ten days later.

On January 16, 1933, at a *fourth operation*, the right premotor area was removed. Marked spasticity of both upper extremities appeared with moderate increase in resistance to passive manipulation, especially of the left extremities. Forced grasping was also marked, and became permanent in both hands, but was ill-defined and transient in the feet. On the second day following operation there was a marked extensor plantar response on the right with fanning of the toes, but this disappeared on the fourth post-operative day. A weak Rossolimo appeared on the right on the second day, and on the left side on the fifth post-operative day. These have increased in magnitude and ease of elicitation, and have remained constant during the two ensuing months; they are still present (April, 1933).

Discussion and Conclusions.

The reflexes which these animals exhibited as a result of the various operative procedures may best be described by stating the phenomena which have been observed after unilateral and bilateral lesions restricted to: Area 4, Area 6, and to Areas 4 and 6 together. It is to be understood that all stated time intervals relate to chimpanzees.

Unilateral Lesions.

(1) *Area* 4.—It has already been pointed out that a lesion sharply restricted to the site of origin of the pyramidal fibres controlling the lower extremity causes a flaccid paralysis with the appearance of a simple unmodified Babinski response, without lateral deviation of the toes. The Chaddock sign is also well developed, and the present observations substantiate those of Schick [20] who found that the Chaddock sign is invariably associated with sign of Babinski in chimpanzees. Tendon reflexes are not exaggerated and the sign of Rossolimo is absent or minimal. Involuntary forced grasping is never seen. The animal recovers its capacity to use the extremity in ordinary locomotor movements quite effectively, but voluntary prehension of the toes is permanently impaired and may be completely absent for one to two months.

(2) *Area* 6.—Lesions restricted to Area 6 may be followed by a transient positive Babinski response which persists for only a day or two. The fanning sign of Babinski, however, may be present for two to three weeks and sometimes longer, but it may be associated with little or no extension of the toes, and in Experiment 2 fanning was accompanied by an increased *flexor* response of the toes. The Rossolimo phenomenon is always well developed and, while it diminishes with time, was present in one chimpanzee for a period of three months following a unilateral lesion. Finally, the symptoms of involuntary grasping evoked by gentle contact of an object with the sole of the foot is strongly present for a period of two to three weeks and then gradually disappears. The extremities opposite a lesion of Area 6 remain moderately spastic for a period of from one to several weeks.

(3) *Areas* 4 *and* 6.—When both Areas 4 and 6 are removed simultaneously, or in sequence, the Babinski response is very greatly enhanced over that seen following lesions restricted to Area 4, and the fanning sign appears as a second and invariable phase of the Babinski. The sign of Rossolimo is present and becomes exaggerated with other tendon reflexes. As far as we are aware it remains permanently. Forced grasping is also present, and if it had appeared when Area 6 was destroyed before Area 4, it does not immediately disappear when the pyramidal representation in the cortex is destroyed. We are aware that this is contrary to impressions gained from the study of clinical cases.

Bilateral Lesions.

When lesions corresponding to the preceding are made on both sides, the symptoms already present as a result of the unilateral lesions become uniformly and often very dramatically exaggerated on the previously affected, *i.e.*, the ipsilateral, side. Indisputable evidence has been obtained in this way of the existence of bilateral representation in both Areas 4 and 6.

Area 4.—When the *motor* representation of the second lower extremity is removed, flaccid paralysis of the contralateral limbs appears, and in addition the symptoms in the previously monoplegic extremity become greatly exaggerated, *i.e.*, motor power is diminished [8, 10], and the Babinski and the Rossolimo signs are increased. Forced grasping and the fan-shaped sign, however, do not appear.

Area 6.—Destruction of the second *premotor* area produces in chimpanzees, as Richter and Hines [17, 18] have found in monkeys, the reappearance of the involuntary grasping reflex on the ipsilateral side

as well as on the contralateral. In our experience the phenomenon does not become permanent in chimpanzees or monkeys until Area 4 has also been destroyed on both sides. The fanning sign is greatly increased in bilateral preparations restricted to Area 6, but it is also transient. The Rossolimo sign, however, becomes permanent after bilateral premotor lesions.

Areas 4 and 6.— We have not yet had the opportunity of studying a chimpanzee in which all of Areas 4 and 6 had been destroyed on both sides, but in the chimpanzee "Mussai" (Experiment 4) all of Area 6 and the part of Area 4 corresponding to the entire motor representation of the upper extremity, was destroyed bilaterally. The animal showed grave and permanent impairment of motor performance of the upper extremities with spasticity and very curious restriction of voluntary movement.

In monkeys and baboons in which Areas 4 and 6 have been completely removed bilaterally the animals have suffered virtually complete and permanent loss of voluntary power in all four extremities; forced grasping [3] and spasticity are also permanent and extreme [11] and the involuntary postural and righting reflexes of Magnus and de Kleyn make their appearance [12]. From the point of view of its postural reflex status such an animal cannot be distinguished from the thalamic monkeys described by Magnus [15] in which both cerebral hemispheres had been completely removed. It is clear, therefore, that Areas 4 and 6 contain the chief, and probably the only volitionally significant motor projection systems from the cortex.

The preceding observations are summarized in the following table :—

TABLE I.—SHOWING EFFECT ON SPASTICITY AND THE PATHOLOGICAL REFLEXES OF UNILATERAL AND BILATERAL LESIONS OF MOTOR AND PREMOTOR AREAS IN THE CHIMPANZEE.

	Spasticity	Babinski Chaddock	Toe fanning	Rossolimo and increase of other tendon reflexes	Forced grasping
Unilateral—					
Area 4	Absent	Permanent	Absent	Absent	Absent*
Area 6	Transient	Absent*	Transient	Permanent	Transient
Area 4 and 6 ..	Permanent	Permanent	Transient or Permanent	Permanent	Transient
Bilateral—					
Area 4	Absent*	Permanent	Absent	Absent	Absent
Area 6	Transient	Absent*	Permanent	Permanent	Transient
Area 4 and 6 ..	Permanent	Permanent	Permanent	Permanent	Permanent

* Occasionally present for 12 to 48 hours after operation, evidently due to disturbances incident to removal of the area closely adjacent.

From these observations it is clear that the two components of the pathological reflex originally described by Babinski are not produced, in the chimpanzee, by lesions of the same cortical area. Lesions restricted to the origin of the pyramidal tract (Area 4) are invariably followed by a simple extensor toe response without fanning or lateral deviation, but when Area 6 is extirpated also there ensues fanning and lateral deviation of the toes, together with a more pronounced extensor response.

In addition, the excitability of the tendon reflexes becomes markedly exaggerated after lesions of Area 6, but not after lesions restricted to the true motor area. This hyperactivity is accompanied by a Rossolimo response, and by the symptom of involuntary forced grasping which is transient in lesions of Area 6 alone, but becomes permanent when 4 and 6 are extirpated together. The Rossolimo response, however, is peculiarly sensitive and may persist indefinitely after a small unilateral lesion.

When the lesions are of such a nature that the more marked symptoms such as spasticity and forced grasping are transient, *i.e.*, in unilateral lesions of Area 6, the positive Rossolimo response persists after the disappearance of all other pathological signs. Similarly in lesions of Areas 4 and 6 the extensor Babinski response and the Rossolimo sign are permanent and are the most outstanding objective evidence of an abnormal condition in the period after ultimate functional recovery has taken place.

Our observations are borne out by those of Schick alluded to above. He found a Rossolimo response in three infant *Macacus rhesus* monkeys during the first month of life at a time when reflex grasping was prominent. In adult macaques the Rossolimo response cannot be obtained. Goldflam [13] made a similar observation in normal human infants during the first month of life. In studying a large group of diseases of the central nervous system in human subjects, Goldflam also has found the Babinski phenomenon frequently present in the absence of the Rossolimo and *vice versa*. After studying the pathological material in connection with this, he concluded that the Rossolimo reflex is a sign of release of function from a pathway other than the pyramidal tract, but which courses beside it in the lateral columns of the cord.

Since our evidence obtained from anthropoid material is in agreement with that of Goldflam on man that the cortical projection systems responsible for the Rossolimo and for the Babinski extensor phenomena are not the same, a further inference may be drawn that, in human

cases of lesions of the cortex, the absence or presence of fanning of the toes, spasticity, and a positive Rossolimo are of value for cortical localization. Presence of a simple extensor Babinski would then be considered as evidence of a lesion restricted to the pyramidal motor system, but a more pronounced extensor response with fanning of the toes and a Rossolimo reflex would suggest a more extensive lesion, involving Area 6 or its projection system from the cortex, which passes through the anterior end of the internal capsule [Poliak 16]. In these circumstances, spasticity would be expected, as well as transient reflex grasping.

It may, therefore, be inferred that the spasticity of a capsular hemiplegia is due to interruption of motor projection systems, from both Areas 4 and 6 (*cf.* Walshe, [21]), and that spasticity is likely to be more pronounced in lesions involving the anterior end of the capsule in addition to the mid-region of the capsule through which the pyramidal fibres pass. Finally, following unilateral lesions, forced grasping and the involuntary postural reflexes of Magnus are transient and become permanent only when the motor projection systems of Areas 4 and 6 from both hemispheres are interrupted [3, 11, 12].

Summary.

The more common neurological signs have been investigated in tame chimpanzees before and after circumscribed surgical lesions of various excitable regions of the cerebral hemispheres. The excitable cortex of the chimpanzee, as well as of man, consists of two principal areas: (i) the region of origin of the pyramidal pathways (Area 4) which lies just anterior to and within the central sulcus, and (ii) the premotor region (Area 6) lying anterior to Area 4, which, through its connections with the pyramidal tracts and with the basal ganglia, red nucleus and other subcortical regions, serves, as we have pointed out elsewhere [11], to correlate postural with volitional adjustments. Our principal conclusions are as follows:—

(1) Lesions of Area 4 cause *flaccid* paralysis of the contralateral extremities, a Babinski response and diminution of tendon reflexes. These signs become more pronounced after bilateral extirpation of Area 4.

(2) Lesions restricted to the premotor area (Area 6) are followed by *spastic* paresis of the contralateral extremities, together with forced grasping, an increase in tendon reflexes, the Rossolimo response and fanning of the toes. These signs are present for a longer period after

bilateral than after *unilateral* lesions of Area 6. Recovery of motor power may be extensive, but the sign of Rossolimo persists permanently, even after a unilateral lesion.

(3) When Areas 4 and 6 are both removed from one cortex, very marked spasticity and forced grasping appear. The extensor Babinski response becomes exaggerated; Rossolimo's sign is increased and tendon reflexes are permanently exaggerated. Motor deficit, moreover, is permanent and grave.

(4) In all cases of removal of a *second* motor or premotor area, the existence of bilateral innervation has been demonstrated by augmentation of the symptoms in the ipsilateral extremities.

(5) In monkeys and baboons, complete bilateral extirpation of Areas 4 and 6 is followed by permanent and complete loss of voluntary power. Forced grasping and spasticity are extreme, and the involuntary postural and righting reflexes of Magnus and de Kleyn may be demonstrated readily. The bodily reflex status of such animals appears to be identical with that of thalamic preparations.

(6) Presence of spasticity, forced grasping, the fanning sign and the Rossolimo tendon reflex of the digits, thus points to lesions involving the premotor area or its projection system from the cortex, while flaccidity, the simple extensor Babinski response and depression of tendon reflexes, suggests a lesion restricted to the pyramidal tract.

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Notices of Recent Publications.

Anatomie médico-chirurgicale du Système nerveux végétatif. Par J. Delmas et G. Laux. Paris: Masson et Cie. 1933. Pp. 266. Price 80 fr.

In an introduction to this monograph Professor Duval claims as a special merit of it the attempt of the authors to subordinate anatomical description to the conception of an active functioning organ. In this task, the desirability of which is obvious to anyone who reads the numerous textbooks on the autonomic system which have recently appeared, they have largely succeeded; they treat, in other words, the vegetative nervous system as a part of a vital machine and do not merely describe it as seen by the anatomist. The anatomy of its various parts does not, however, suffer from this mode of approach; the relations and connections of the sympathetic ganglia and pathways are clearly but concisely described and illustrated copiously by admirably reproduced plates, as well as by numerous diagrammatic drawings. In their efforts at systematization, as in dealing with the higher centres grouped around the thalamus and third ventricle, they may go beyond definitely established facts, but they are judicious in the use of hypotheses and careful to point out where more evidence is necessary before their views can be definitely accepted. The volume is, unlike many textbooks on the anatomy of the nervous system, obviously based largely on original work and has therefore a personal character which adds to its value. The last section, which is also excellently illustrated, contains descriptions of methods of surgical approach to the more important parts of the vegetative system.

It is admirable both as a textbook and a work of reference, and in the latter respect the bibliography, though it contains mainly French references, will be useful, while if the surgery of this portion of the nervous system ever acquires the importance which the authors tacitly assume it has now, it will be of further service.

Études neurologiques. 5me Série. Par G. Guillain. Paris: Masson et Cie. 1932. P. 462. Price 80 fr.

We can extend to the fifth volume of his collected papers the same welcome that we offered to Professor Guillain's earlier volumes. This, as those which preceded it, contains reprints of articles published in various journals or in the records of clinical societies by the chief of the Salpêtrière and his assistants: they are consequently of unequal value, some being merely short notes or clinical descriptions, but others are more elaborate contributions.

As in the previous collections the articles are arranged according to the subjects with which they deal. An index would have made it more useful for the purpose of reference.

Beiträge zur Kenntnis der Narkolepsie. Von R. THIELE und H. BERNHARDT. Berlin: S. Karger. 1933. S. 187. Price 18 M.

A series of thirty-five personally observed cases is described, together with the records of seriological and radiographic investigations.

The clinical picture of narcolepsy as observed by the authors and described in the literature is summarized and discussed. There is a lengthy and speculative chapter on aetiology and pathogenesis from which no new facts emerge. By way of treatment the use of ephedrin is recommended as sometimes of value in reducing the frequency of the attacks of sleep, though the authors have found it ineffective in the case of cataplexy.

Hirn und Ohr. von K. GRAHE. Leipzig: G. Thieme. 1932. S. 108. Price 9.60 M.

The accurate examination of hearing and of the functions of the vestibular apparatus has not as a rule received in neurology the attention it deserves. This small book is timely as it shows what information may be sometimes obtained by such investigations, and as in it the author describes concisely and clearly the methods of making them. It is the chapter on the methods of examination which will be of most value to the neurologist, for by a study of it he can easily learn to carry them out himself and not refer his patients for this purpose to an otologist, a common but not very satisfactory arrangement.

The description of the disturbances of these functions by various peripheral and central lesions shows what information may be obtained, but the conclusions drawn from them need critical evaluation from the neurological point of view.

Moderne Therapie der Neurosyphilis. von B. DATTNER. Wien: W. Maudrich. 1933. S. 334. Price 22 M.

The earlier chapters of this volume describe in detail the pathological investigations necessary for the diagnosis of neurosyphilis, as the examination of the cerebrospinal fluid, and discuss fully their value and significance. The greater part of it is, however, devoted to questions of treatment, the general principles being first discussed and later the treatment of the more important diseases, as dementia paralytica and tabes. The reader will be introduced to many drugs scarcely known in this country, and, as might be expected of an author of the Vienna school, great emphasis is also laid on fever-producing methods, as infection by malaria, recurrent fever and rat-bite fever. This monograph is an exceptionally important contribution to the subject with which it deals.

Alcohol and Man. The Effects of Alcohol on Man in Health and Disease. Edited by H. EMERSON, etc. New York: The Macmillan Co. 1932. Pp. 451. Price 18s.

The age-long discussion on the effects of alcohol on man is taken up here again by a group of writers, clinical, physiological, pharmacological, psychiatric, statistical and others, each of whom is responsible for a separate section in which he expresses his views based on his own work and experience. Every part of the subject is adequately covered, and though each author is writing independently of the others the various chapters are so well edited and arranged that as a whole the book is easily read, while, on the other hand, any part of the subject may be readily referred to in it. The aim of the editor has been to present to the educated layman such facts and opinions on the influence of alcohol in either moderate or excessive amounts as appear sufficiently established from the social and biological as well as from the medical point of view. He has succeeded in producing a volume which can be recommended to all interested in this important subject.

An Introduction to Analytical Psychotherapy. By T. A. ROSS. London: Edward Arnold. 1932. Pp. 203. Price 10s. 6d.

This book rests on a wide experience, and is honest, clear and reasoned. But it is written so sensibly, its author has so wisely refrained from extravagant or over-subtle interpretations, that one is apt to ignore the intellectually unsatisfying nature of the moderate theory put forward and its implications, if logically pursued. This is, however, no defect, since the pragmatic test is decisive in psychotherapy, if anywhere: and it is well known that the author of this work is a most successful psychotherapist. As Prinzhorn and many others have pointed out, there is a wide gulf between the methods efficacious in mental healing and those of medicine generally, the personality of the physician and his relationship to the patient being decisive in the former, while his theory and mode of procedure are of minor importance. As the brevity of the chapter on technique shows, practical psychotherapy cannot be set down in a scheme or taught: it must be learnt by personal experience in one's work with patients, and to those who wish for guidance in this empirical training Dr. Ross's book will prove of value.

Éther, Cocaine, Hachich, Peyotl et Démence précoce. Essai d'Exploration pharmacodynamique du Psychisme des Déments précoces. Par ANDRÉE DESCHAMPS. Paris: Les Éditions Vega. 1932. Pp. 210.

The influence of drugs such as amytal and carbon monoxide on catatonic states has received much attention in the last few years, as has also the study of abnormal states produced in healthy people by mescalin, hashish, etc. The author of this monograph, prompted and directed by his teacher C. Pascal, has

given to thirty-two patients with gross schizophrenic features ether, cocaine, caffeine and hashish, either alone or, as in most cases, combined: two patients were given peyotl. Improvement in the drugged state was found in the cases with a better prognosis. Where a previously mute patient spoke while under the influence of the drugs, his thought seemed to show features distinct from what is found in toxic states or in archaic modes of thinking. Therapeutic applications of the method are suggested and numerous points in psychopathology are dealt with. As a whole the monograph has an amateurish stamp; the examination of the evidence is rather superficial and uncritical, but there is much of interest in the research.

Naturgeschichte der Seele und Ihres Bewusstwerdens: Mnemistische Biopsychologie. von EUGEN BLEULER. Zweite Auflage. Berlin: Springer. 1932. Pp. 268. Price Rm. 16.

This second edition of Professor Bleuler's book may be set alongside the last production of another distinguished Swiss, von Monakow, as an ordered attempt to sum up human psychology from a biological point of view. The method used is that of the natural sciences; and the too-familiar insistence on the alleged conceptual necessity for a cleavage between physical and psychical is repudiated. The presentation of this way of regarding human activity is slightly modified from that of the first edition, especially in regard to consciousness and perception. In an energetic foreword Bleuler examines and rejects some criticisms which came chiefly from philosophers. The body of the work deals with the derivation of consciousness from the integrated function of the central nervous system and with the apparatus of the mind. This erudite and complicated design for a mnemistic psychology is a notable contribution towards the understanding of the relation between mental functions and the total activity of the central nervous system.

Allgemeine Neurosenlehre auf psychoanalytischer Grundlage. von HERMANN NUNBERG. Bern: Huber. 1932. Pp. 339. Price Sv. Fr. 15.

There have hitherto been available only two fairly comprehensive and adequate formulations of the body of psycho-analytic doctrine, Freud's "Introductory Lectures" and the non-committal Healy-Bronner-Bowers volume. The present work may be accepted as an authoritative and better-organized account of the opinions now held in the Viennese stronghold of psycho-analysis; Freud, in his brief preface, calls the book "the most complete and conscientious presentation of a psycho-analytic theory of neurotic processes that we have." Such an imprimatur makes the book valuable in a field so much at the mercy of dogmatism and wordy speculation; one can here examine the theory and method of psycho-analysis as acknowledged by its founder. At some points there is considerable divergence from the views now

current in the English school, but this may not be a disadvantage. The book is coherent and well arranged, but there is much repetition. On the whole, where it is difficult to read this is due not so much to its style as to its subject and mode of thought. It is noteworthy that in a book of 312 pages, only 19 are specifically devoted to the theoretical basis of therapy.

Human Values in Psychological Medicine. By C. P. Blacker, London: Oxford University Press. Humphrey Milford. 1933. Pp. 179.

Philosophical speculations about psychology and mental disorder are usually jejune and often ill-informed: but to this book, written by an experienced psychiatrist, no such objection can be made. It is, on the contrary, stimulating and sound. The author has applied to his clinical material a general theory in which human idiosynerasy, the groundwork of medical psychology, is regarded as lying mainly in the realm of affective life and expressing itself in the individual's values. The biological implications and development of the author's views are set forth with especial vigour in the valuable chapter on life and death instincts, in which the Freudian teachings on the subject are discussed. In the body of the book the phenomena of mental life, both normal and morbid, are reviewed in the light of the general theory, and an interpretation of them offered which has the merit of lucidity, cohesion and a just biological foundation.

Das Rechtsgefühl. von A. E. Hoche. Berlin: Springer. 1932. Pp. 102. Price Rm. 5.80.

This small book embodies the views of one of the most distinguished of German psychiatrists of the last generation who has latterly occupied himself chiefly with the forensic and social bearings of his subject. He here discusses the psychology of social justice, of the feelings on which equity and right are based for the individual. The psychiatric significance of this is seen in paranoid states and in certain forms of psychopathic personality. The author, however, enlarges his theme to cover questions of politics: the book is informed by a conception of human rights to which the recent developments in Germany are an ironical commentary. The book is written with great clearness of thought and diction, and is an interesting contribution to social psychology.

Emigration and Insanity. By Örnulv Ödegaard. Copenhagen: Levin and Munksgaard. 1932. Pp. 206.

The study of racial psychiatry is a difficult field in which linguistic and cultural obstacles or political prejudices make the observations of most writers as questionable as their conclusions. Dr. Ödegaard's investigation, however,

is a model of what such a study should be. He has compared the incidence of mental disorder in the Norwegian-born population of Minnesota with that in Norway and has considered the relevant social problems. He finds that exogenous factors are more significant in the psychoses of immigrants than constitutional ones, and he accounts for the relative frequency of schizophrenia among them by supposing that a schizoid personality predisposes to restlessness and so to emigration. The strain of immigrant life does not seem to have played a part in the causation of the endogenous psychoses. The work is presented clearly, though in considerable detail, and is of anthropological, as well as psychiatric, importance.

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EDITOR.